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NEWS 5	Aug 19	Aquatic Toxicity Information Retrieval (AQUIRE) now available on STN
NEWS 6	Aug 26	Sequence searching in REGISTRY enhanced
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NEWS 10	Oct 01	CASREACT Enriched with Reactions from 1907 to 1985
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NEWS 14	Nov 25	More calculated properties added to REGISTRY
NEWS 15	Dec 04	CSA files on STN
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NEWS 18	Dec 17	Adis Clinical Trials Insight now available on STN
NEWS 19	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS 20	Feb 13	CANCERLIT is no longer being updated
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NEWS 24	Feb 26	NTIS now allows simultaneous left and right truncation
NEWS 25	Feb 26	PCTFULL now contains images
NEWS 26	Mar 04	SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27	Mar 19	APOLLIT offering free connect time in April 2003
NEWS 28	Mar 20	EVENTLINE will be removed from STN
NEWS 29	Mar 24	PATDPAFULL now available on STN
NEWS 30	Mar 24	Additional information for trade-named substances without structures available in REGISTRY
NEWS 31	Apr 11	Display formats in DGENE enhanced
NEWS 32	Apr 14	MEDLINE Reload
NEWS 33	Apr 17	Polymer searching in REGISTRY enhanced
NEWS 34	Apr 21	Indexing from 1947 to 1956 being added to records in CA/CAPLUS
NEWS 35	Apr 21	New current-awareness alert (SDI) frequency in WPIDS/WPINDEX/WPIX
NEWS 36	Apr 28	RDISCLOSURE now available on STN
NEWS 37	May 05	Pharmacokinetic information and systematic chemical names added to PHAR

NEWS EXPRESS	April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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=> s (venezuelan equine encephalitis virus) or VEE
L1         2090 (VENEZUELAN EQUINE ENCEPHALITIS VIRUS) OR VEE

=> s capsid
L2        41672 CAPSID

=> s l1 and l2
L3          123 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4            57 DUP REM L3 (66 DUPLICATES REMOVED)

=> d ti l4 1-10

L4   ANSWER 1 OF 57  CAPLUS  COPYRIGHT 2003 ACS
TI   Alphavirus replicon vector systems

L4   ANSWER 2 OF 57  CAPLUS  COPYRIGHT 2003 ACS
```

TI Structure of isolated nucleocapsids from **Venezuelan equine encephalitis virus** and implications for assembly and disassembly of enveloped virus

L4 ANSWER 3 OF 57 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI Novel chimeric alphavirus particle, useful for generating an immune response in a mammal, has RNA derived from one or more alphaviruses, and structural proteins derived from two or more alphaviruses;
recombinant virus particle and vector expression in host cell for use in gene therapy

L4 ANSWER 4 OF 57 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI New recombinant polynucleotides encoding positive-strand RNA virus structural proteins useful for creating virus-based (e.g. poxvirus) replicon particle packaging systems for use in recombinant protein synthesis or gene therapy;
virus vector-mediated gene transfer, and expression in BHK21 or FrhL cell culture, useful for tumor gene therapy, immunotherapy and as a recombinant vaccine

L4 ANSWER 5 OF 57 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI Eukaryotic layered vector initiation system, for gene therapy, has alphaviral nonstructural protein gene having mutant nonstructural protein 2 gene, which reduces host-cell directed macromolecular synthesis;
recombinant virus vector expression in host cell for use in gene therapy

L4 ANSWER 6 OF 57 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI A western equine encephalitis (WEE) virus strain used to develop DNA vaccines to WEE virus and related alphaviruses;
virus vaccine, vector expression in host cell use in gene therapy

L4 ANSWER 7 OF 57 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI A new recombinant alphavirus particle comprising an alphavirus vector which directs expression of a heterologous gene, a **capsid** protein and an envelope glycoprotein from a different virus is useful in gene therapy;
recombinant virus vector-mediated **capsid** protein and envelope glycoprotein gene transfer and expression in host cell for use in gene therapy

L4 ANSWER 8 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Alphavirus particles for gene therapy carrying domain-exchanged **capsid** protein or envelope glycoproteins fusion products

L4 ANSWER 9 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Packaging of replication-defective positive-strand RNA virus particles using poxvirus helper virus

L4 ANSWER 10 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Crystal structure of VEEV **capsid** protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug screening

=> d ti l4 11-30

L4 ANSWER 11 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI Binding of Norwalk virus-like particles to ABH histo-blood group antigens is blocked by antisera from infected human volunteers or experimentally vaccinated mice.

L4 ANSWER 12 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Vector infection determinants of **Venezuelan equine**

encephalitis virus reside within the E2 envelope glycoprotein

L4 ANSWER 13 OF 57 MEDLINE DUPLICATE 1
TI Comparison of two aquatic alphaviruses, salmon pancreas disease virus and sleeping disease virus, by using genome sequence analysis, monoclonal reactivity, and cross-infection.

L4 ANSWER 14 OF 57 MEDLINE DUPLICATE 2
TI Expression and self-assembly of norwalk virus **capsid** protein from **venezuelan equine encephalitis virus** replicons.

L4 ANSWER 15 OF 57 MEDLINE DUPLICATE 3
TI Systemic, mucosal, and heterotypic immune induction in mice inoculated with Venezuelan equine encephalitis replicons expressing Norwalk virus-like particles.

L4 ANSWER 16 OF 57 MEDLINE DUPLICATE 4
TI Alphavirus replicon particles as candidate HIV vaccines.

L4 ANSWER 17 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Compositions and methods for packaging of alphavirus vectors

L4 ANSWER 18 OF 57 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI Attenuated **Venezuelan equine encephalitis virus** useful as a vaccine contains a rearrangement in genome such that its structural glycoproteins precede the **capsid** gene; Venezuelan-horse-encephalitis virus attenuation for use as a recombinant vaccine, DNA primer for use in disease diagnosis and antibody for use in therapy

L4 ANSWER 19 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Compositions and methods for packaging of alphavirus vectors

L4 ANSWER 20 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Live attenuated **venezuelan equine encephalitis virus** (**VEE**) vaccine using recombinant **VEE** containing inserted sequences in the viral genome between its glycoprotein gene and **capsid** gene

L4 ANSWER 21 OF 57 MEDLINE DUPLICATE 5
TI Core protein-coding sequence, but not core protein, modulates the efficiency of cap-independent translation directed by the internal ribosome entry site of hepatitis C virus.

L4 ANSWER 22 OF 57 MEDLINE DUPLICATE 6
TI Expression of the two major envelope proteins of equine arteritis virus as a heterodimer is necessary for induction of neutralizing antibodies in mice immunized with recombinant **Venezuelan equine encephalitis virus** replicon particles.

L4 ANSWER 23 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI SIV and HIV vaccines using **VEE** replicon particles

L4 ANSWER 24 OF 57 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI New deletion mutant of **Venezuelan-equine-encephalitis virus**, useful as vaccine; adeno virus, vaccinia virus or plasmid vector-mediated Venezuelan-horse-encephalitis virus gene transfer and expression, used for nucleic acid vaccine and gene therapy

L4 ANSWER 25 OF 57 MEDLINE DUPLICATE 8
TI Genetic and phenotypic changes accompanying the emergence of epizootic

subtype IC Venezuelan equine encephalitis viruses from an enzootic subtype ID progenitor.

L4 ANSWER 26 OF 57 MEDLINE DUPLICATE 9
TI **Venezuelan equine encephalitis virus** vectors expressing HIV-1 proteins: vector design strategies for improved vaccine efficacy.

L4 ANSWER 27 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI The HPLC separation and chemical characterization of proteins from tick-borne encephalitis and Venezuelan equine encephalomyelitis viruses

L4 ANSWER 28 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Multivalent vector vaccines for bacterial and viral infections of horses

L4 ANSWER 29 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Viral Characterization by Direct Analysis of **Capsid** Proteins

L4 ANSWER 30 OF 57 MEDLINE DUPLICATE 10
TI Nucleotide sequences of the 26S mRNAs of the viruses defining the Venezuelan equine encephalitis antigenic complex.

=> d ti l4 31-57

L4 ANSWER 31 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Recombinant alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis

L4 ANSWER 32 OF 57 MEDLINE DUPLICATE 11
TI Humoral, mucosal, and cellular immunity in response to a human immunodeficiency virus type 1 immunogen expressed by a **Venezuelan equine encephalitis virus** vaccine vector.

L4 ANSWER 33 OF 57 MEDLINE DUPLICATE 12
TI Replicon-helper systems from attenuated **Venezuelan equine encephalitis virus**: expression of heterologous genes in vitro and immunization against heterologous pathogens in vivo.

L4 ANSWER 34 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Helper cells and RNAs for producing infectious, replication-defective alphavirus particles for vaccination

L4 ANSWER 35 OF 57 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI Development of a generic vaccine delivery system based on a Venezuelan-equine-encephalitis (**VEE**) virus replicon; Venezuelan-horse-encephalitis virus vector attenuation for recombinant vaccine construction (conference abstract)

L4 ANSWER 36 OF 57 MEDLINE DUPLICATE 13
TI Murine T-helper cell immune response to recombinant vaccinia-**Venezuelan equine encephalitis virus**

L4 ANSWER 37 OF 57 MEDLINE
TI Localization of four antigenic sites involved in Venezuelan equine encephalomyelitis virus protection.

L4 ANSWER 38 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Recombinant Venezuelan equine encephalomyelitis viruses expressing HBsAg

L4 ANSWER 39 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI A comparison of the nucleotide sequences of eastern and western equine

encephalomyelitis viruses with those of other alphaviruses and related RNA viruses.

L4 ANSWER 40 OF 57 MEDLINE DUPLICATE 14
TI Immunogens of encephalitis viruses.

L4 ANSWER 41 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Effect of mutations in structural protein genes on attenuation of **Venezuelan equine encephalitis virus**

L4 ANSWER 42 OF 57 CAPLUS COPYRIGHT 2003 ACS
TI Genetic evidence that epizootic Venezuelan equine encephalitis (**VEE**) viruses may have evolved from enzootic **VEE** subtype I-D virus

L4 ANSWER 43 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI COMPLETE SEQUENCE OF THE GENOMIC RNA OF O'NYONG-NYONG VIRUS AND ITS USE IN THE CONSTRUCTION OF ALPHAVIRUS PHYLOGENETIC TREES.

L4 ANSWER 44 OF 57 MEDLINE
TI In vitro synthesis of infectious **venezuelan equine encephalitis virus** RNA from a cDNA clone: analysis of a viable deletion mutant.

L4 ANSWER 45 OF 57 MEDLINE DUPLICATE 15
TI The full-length nucleotide sequences of the virulent Trinidad donkey strain of **Venezuelan equine encephalitis virus** and its attenuated vaccine derivative, strain TC-83.

L4 ANSWER 46 OF 57 MEDLINE DUPLICATE 16
TI Recombinant vaccinia virus/Venezuelan equine encephalitis (**VEE**) virus protects mice from peripheral **VEE** virus challenge.

L4 ANSWER 47 OF 57 MEDLINE DUPLICATE 17
TI Recombinant vaccinia/Venezuelan equine encephalitis (**VEE**) virus expresses **VEE** structural proteins.

L4 ANSWER 48 OF 57 MEDLINE DUPLICATE 18
TI Nucleotide sequence of the genome region encoding the 26S mRNA of eastern equine encephalomyelitis virus and the deduced amino acid sequence of the viral structural proteins.

L4 ANSWER 49 OF 57 MEDLINE DUPLICATE 19
TI Molecular determinants of alphavirus neurovirulence: nucleotide and deduced protein sequence changes during attenuation of **Venezuelan equine encephalitis virus**.

L4 ANSWER 50 OF 57 MEDLINE DUPLICATE 20
TI Nucleotide sequence of the 26 S mRNA of the virulent Trinidad donkey strain of **Venezuelan equine encephalitis virus** and deduced sequence of the encoded structural proteins.

L4 ANSWER 51 OF 57 MEDLINE DUPLICATE 21
TI Comparative immunological and biochemical analyses of viruses in the Venezuelan equine encephalitis complex.

L4 ANSWER 52 OF 57 MEDLINE DUPLICATE 22
TI Identification of a new **Venezuelan equine encephalitis virus** from Brazil.

L4 ANSWER 53 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 23
TI CONSERVATION OF TRYPTIC PEPTIDES IN THE STRUCTURAL PROTEINS OF VIRUSES IN THE VENEZUELAN EQUINE ENCEPHALITIS COMPLEX.

L4 ANSWER 54 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 24
TI ANTIGENIC ANALYSIS OF THE SURFACE GLYCO PROTEINS OF A VENEZUELAN EQUINE ENCEPHALOMYELITIS VIRUS TC-83 USING MONO CLONAL ANTIBODIES.

L4 ANSWER 55 OF 57 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI A COMPARISON OF THE 26S MESSENGER RNA AND STRUCTURAL PROTEINS OF AN EQUINE VIRULENT VENEZUELAN ENCEPHALITIS VIRUS AND ITS VACCINE DERIVATIVE.

L4 ANSWER 56 OF 57 MEDLINE DUPLICATE 25
TI Tetracycline-mediated photodynamic inactivation of animal viruses.

L4 ANSWER 57 OF 57 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI Venezuelan equine encephalomyelitis virus: structural components.

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FULL ESTIMATED COST	30.56	30.77

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=> s venezuelan and (capsid protein)
L5 80 VENEZUELAN AND (CAPSID PROTEIN)

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 39 DUP REM L5 (41 DUPLICATES REMOVED)

=> d ti l6 1-39

L6 ANSWER 1 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Alphavirus replicon vector systems

L6 ANSWER 2 OF 39 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI Novel chimeric alphavirus particle, useful for generating an immune response in a mammal, has RNA derived from one or more alphaviruses, and structural proteins derived from two or more alphaviruses;
recombinant virus particle and vector expression in host cell for use in gene therapy

L6 ANSWER 3 OF 39 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI A new recombinant alphavirus particle comprising an alphavirus vector which directs expression of a heterologous gene, a **capsid protein** and an envelope glycoprotein from a different virus is useful in gene therapy;
recombinant virus vector-mediated **capsid protein** and envelope glycoprotein gene transfer and expression in host cell

for use in gene therapy

L6 ANSWER 4 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Alphavirus particles for gene therapy carrying domain-exchanged **capsid protein** or envelope glycoproteins fusion products

L6 ANSWER 5 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Crystal structure of VEEV **capsid protein** C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug screening

L6 ANSWER 6 OF 39 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
TI Binding of Norwalk virus-like particles to ABH histo-blood group antigens is blocked by antisera from infected human volunteers or experimentally vaccinated mice.

L6 ANSWER 7 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
TI Comparison of two aquatic alphaviruses, salmon pancreas disease virus and sleeping disease virus, by using genome sequence analysis, monoclonal reactivity, and cross-infection.

L6 ANSWER 8 OF 39 MEDLINE DUPLICATE 2
TI Expression and self-assembly of norwalk virus **capsid protein** from **venezuelan** equine encephalitis virus replicons.

L6 ANSWER 9 OF 39 MEDLINE DUPLICATE 3
TI Systemic, mucosal, and heterotypic immune induction in mice inoculated with **Venezuelan** equine encephalitis replicons expressing Norwalk virus-like particles.

L6 ANSWER 10 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Compositions and methods for packaging of alphavirus vectors

L6 ANSWER 11 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Compositions and methods for packaging of alphavirus vectors

L6 ANSWER 12 OF 39 MEDLINE DUPLICATE 4
TI Core protein-coding sequence, but not core protein, modulates the efficiency of cap-independent translation directed by the internal ribosome entry site of hepatitis C virus.

L6 ANSWER 13 OF 39 MEDLINE DUPLICATE 5
TI Expression of the two major envelope proteins of equine arteritis virus as a heterodimer is necessary for induction of neutralizing antibodies in mice immunized with recombinant **Venezuelan** equine encephalitis virus replicon particles.

L6 ANSWER 14 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Recombinant viral vaccine for alphaviruses attenuated by deletion of the nuclear targeting signal

L6 ANSWER 15 OF 39 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI **Venezuelan** equine encephalitis virus vectors expressing HIV-1 proteins: vector design strategies for improved vaccine efficacy; **Venezuelan**-horse-encephalitis virus vector encoding HIV virus-1 matrix/**capsid protein**, and optimization as a nucleic acid vaccine

L6 ANSWER 16 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Viral Characterization by Direct Analysis of Capsid Proteins

L6 ANSWER 17 OF 39 CAPLUS COPYRIGHT 2003 ACS

TI Recombinant alphavirus-based vectors with reduced inhibition of cellular macromolecular synthesis

L6 ANSWER 18 OF 39 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI Humoral, mucosal and cellular immunity in response to a human immunodeficiency virus type-1 immunogen expressed by a **Venezuelan** -equine-encephalitis virus vaccine vector;
HIV virus-1 recombinant vaccine expression in BHK cell culture

L6 ANSWER 19 OF 39 MEDLINE DUPLICATE 7
TI Replicon-helper systems from attenuated **Venezuelan** equine encephalitis virus: expression of heterologous genes in vitro and immunization against heterologous pathogens in vivo.

L6 ANSWER 20 OF 39 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
TI Alpha virus RNA helper cells;
Venezuelan-horse-encephalitis virus, Sindbis virus, Semliki-Forest virus attenuation and recombinant vaccine particle production in packaging cell culture

L6 ANSWER 21 OF 39 MEDLINE DUPLICATE 8
TI Comparative amino acid sequence analysis of the major outer **capsid protein** (VP7) of porcine rotaviruses with G3 and G5 serotype specificities isolated in Venezuela and Argentina.

L6 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Recombinant **Venezuelan** equine encephalomyelitis viruses expressing HBsAg

L6 ANSWER 23 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Effect of mutations in structural protein genes on attenuation of **Venezuelan** equine encephalitis virus

L6 ANSWER 24 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Complete sequence of the genomic RNA of O'Nyong-nyong virus and its use in the construction of alphavirus phylogenetic trees

L6 ANSWER 25 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI The full-length nucleotide sequences of the virulent Trinidad donkey strain of **Venezuelan** equine encephalitis virus and its attenuated vaccine derivative, strain TC-83

L6 ANSWER 26 OF 39 MEDLINE DUPLICATE 9
TI Recombinant vaccinia virus/**Venezuelan** equine encephalitis (VEE) virus protects mice from peripheral VEE virus challenge.

L6 ANSWER 27 OF 39 MEDLINE DUPLICATE 10
TI Recombinant vaccinia/**Venezuelan** equine encephalitis (VEE) virus expresses VEE structural proteins.

L6 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Nucleotide sequence of the genome region encoding the 26S mRNA of eastern equine encephalomyelitis virus and the deduced amino acid sequence of the viral structural proteins

L6 ANSWER 29 OF 39 MEDLINE DUPLICATE 11
TI Genetic relatedness among human rotavirus genes coding for VP7, a major neutralization protein, and its application to serotype identification.

L6 ANSWER 30 OF 39 CAPLUS COPYRIGHT 2003 ACS
TI Molecular determinants of alphavirus neurovirulence: nucleotide and deduced protein sequence changes during attenuation of **Venezuelan** equine encephalitis virus

L6 ANSWER 31 OF 39 MEDLINE DUPLICATE 12
TI [Isolation of glycoproteins of the **Venezuelan** equine encephalomyelitis virus and an evaluation of their immunogenic activity]. Vydelenie glikoproteidov virusa venesuel'skogo entsefalomielita loshadei i otsenka ikh immunogennoi aktivnosti.

L6 ANSWER 32 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 13
TI MECHANICAL TRANSMISSION PURIFICATION AND PROPERTIES OF AN ISOLATE OF MAIZE STRIPE VIRUS FROM VENEZUELA.

L6 ANSWER 33 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI PURIFICATION AND PARTIAL CHARACTERIZATION OF PAPAYA RINGSPOT VIRUS.

L6 ANSWER 34 OF 39 MEDLINE DUPLICATE 14
TI Comparative immunological and biochemical analyses of viruses in the **Venezuelan** equine encephalitis complex.

L6 ANSWER 35 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI IDENTIFICATION OF A NEW **VENEZUELAN** EQUINE ENCEPHALITIS VIRUS FROM BRAZIL.

L6 ANSWER 36 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 15
TI CONSERVATION OF TRYPTIC PEPTIDES IN THE STRUCTURAL PROTEINS OF VIRUSES IN THE **VENEZUELAN** EQUINE ENCEPHALITIS COMPLEX.

L6 ANSWER 37 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI A COMPARISON OF THE 26S MESSENGER RNA AND STRUCTURAL PROTEINS OF AN EQUINE VIRULENT **VENEZUELAN** ENCEPHALITIS VIRUS AND ITS VACCINE DERIVATIVE.

L6 ANSWER 38 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
TI CONSERVATION OF TRYPTIC PEPTIDES IN THE STRUCTURAL PROTEINS OF VIRUSES IN THE **VENEZUELAN** EQUINE ENCEPHALITIS COMPLEX.

L6 ANSWER 39 OF 39 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 16
TI HETEROGENEITY OF ENVELOPE POLY PEPTIDES AMONG STRAINS OF **VENEZUELAN** ENCEPHALITIS VIRUS.

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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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FILE 'BIOSIS' ENTERED AT 12:51:44 ON 12 MAY 2003
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FILE 'BIOTECHDS' ENTERED AT 12:51:44 ON 12 MAY 2003
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=> s (venezuelan equine encephalitis virus) or VEE
L1         2090 (VENEZUELAN EQUINE ENCEPHALITIS VIRUS) OR VEE

=> cell (a) death
CELL IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s cell (a) death
L2       168238 CELL (A) DEATH

=> s l1 and l2
L3            9 L1 AND L2

=> d iall l3 1-9

L3   ANSWER 1 OF 9     MEDLINE
ACCESSION NUMBER:    97267881     MEDLINE
DOCUMENT NUMBER:     97267881   PubMed ID: 9113200
TITLE:               Apoptotic cell death is an important
                     cause of neuronal injury in experimental Venezuelan
                     equine encephalitis virus
```

infection of mice.
AUTHOR: Jackson A C; Rossiter J P
CORPORATE SOURCE: Department of Medicine, Queen's University, Ontario, Canada.. jacksona@post.queensu.ca
SOURCE: ACTA NEUROPATHOLOGICA, (1997 Apr) 93 (4) 349-53. Journal code: 0412041. ISSN: 0001-6322.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 19970630
Last Updated on STN: 19970630
Entered Medline: 19970617

ABSTRACT:
Mice develop a fatal encephalomyelitis after infection with the Trinidad donkey strain of Venezuelan equine encephalitis (**VEE**) virus. Adult mice were inoculated intraperitoneally with **VEE** virus and the brains were examined at different time points. Morphological changes were assessed by histological staining. **VEE** virus antigen was detected with immunoperoxidase staining, and DNA fragmentation was evaluated in situ using the terminal deoxynucleotidyl transferase-mediated dUTP-digoxigenin nick end labeling (TUNEL) method. **VEE** antigen was found in many areas of the brain and it was prominent in neurons. There were mild associated inflammatory changes. DNA fragmentation was demonstrated in many of these areas using TUNEL. In areas with TUNEL staining, morphological neuronal changes ranged from nuclear chromatin condensations to nuclear and cellular fragmentation, which are characteristic of apoptosis. There is strong morphological and biochemical evidence of apoptotic **cell death** in this experimental model of **VEE** virus infection.

CONTROLLED TERM: Check Tags: Animal; Male; Support, Non-U.S. Gov't
Antigens, Viral: AN, analysis
*Apoptosis
Brain: PA, pathology
Brain: VI, virology
DNA Fragmentation
DNA Nucleotidylexotransferase
Encephalitis Virus, Venezuelan Equine: IM, immunology
Encephalomyelitis, Venezuelan Equine: ET, etiology
*Encephalomyelitis, Venezuelan Equine: PA, pathology
Encephalomyelitis, Venezuelan Equine: VI, virology
Immunohistochemistry
Mice
Mice, Inbred C57BL
*Neurons: PA, pathology
Neurons: VI, virology
CHEMICAL NAME: 0 (Antigens, Viral); EC 2.7.7.31 (DNA Nucleotidylexotransferase)

L3 ANSWER 2 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1997:213435 BIOSIS
DOCUMENT NUMBER: PREV199799519939
TITLE: Apoptotic **cell death** is an important cause of neuronal injury in experimental **Venezuelan equine encephalitis virus** infection of mice.
AUTHOR(S): Jackson, Alan C. (1); Rossiter, John P.
CORPORATE SOURCE: (1) Dep. Med., Queen's Univ., 78 Barrie St. Kingston, ON K7L 3J7 Canada
SOURCE: Acta Neuropathologica, (1997) Vol. 93, No. 4, pp. 349-353. ISSN: 0001-6322.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:

Mice develop a fatal encephalomyelitis after infection with the Trinidad donkey strain of Venezuelan equine encephalitis (**VEE**) virus. Adult mice were inoculated intraperitoneally with **VEE** virus and the brains were examined at different time points. Morphological changes were assessed by histological staining. **VEE** virus antigen was detected with immunoperoxidase staining, and DNA fragmentation was evaluated in situ using the terminal deoxynucleotidyl transferase-mediated dUTP-digoxigenin nick end labeling (TUNEL) method. **VEE** antigen was found in many areas of the brain and it was prominent in neurons. There were mild associated inflammatory changes. DNA fragmentation was demonstrated in many of these areas using TUNEL. In areas with TUNEL staining, morphological neuronal changes ranged from nuclear chromatin condensations to nuclear and cellular fragmentation, which are characteristic of apoptosis. There is strong morphological and biochemical evidence of apoptotic **cell death** in this experimental model of **VEE** virus infection.

CONCEPT CODE: Cytology and Cytochemistry - Animal *02506
Pathology, General and Miscellaneous - Necrosis *12510
Nervous System - Pathology *20506
Medical and Clinical Microbiology - Virology *36006

BIOSYSTEMATIC CODE: Togaviridae 02626
Muridae *86375

INDEX TERMS: Major Concepts
Cell Biology; Infection; Nervous System (Neural Coordination); Pathology

INDEX TERMS: Miscellaneous Descriptors
APOPTOTIC **CELL DEATH**; BRAIN; EXPERIMENTAL INFECTION; HOST; INFECTION; MORPHOLOGICAL CHANGES; NERVOUS SYSTEM; NEURONAL INJURY; PATHOGEN; STRAIN-TRINIDAD DONKEY; **VENEZUELAN EQUINE ENCEPHALITIS VIRUS** INFECTION; VIRAL DISEASE

ORGANISM: Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Togaviridae: Viruses

ORGANISM: Organism Name
mouse (Muridae); **Venezuelan equine encephalitis virus** (Togaviridae)

ORGANISM: Organism Superterms
animals; chordates; mammals; microorganisms; nonhuman mammals; nonhuman vertebrates; rodents; vertebrates; viruses

L3 ANSWER 3 OF 9 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI

ACCESSION NUMBER: 2003-07981 BIOTECHDS

TITLE: Eukaryotic layered vector initiation system, for gene therapy, has alphaviral nonstructural protein gene having mutant nonstructural protein 2 gene, which reduces host-cell directed macromolecular synthesis;
recombinant virus vector expression in host cell for use in gene therapy

AUTHOR: DUBENSKY T W; POLO J M; BELLI B A; SCHLESINGER S; DRYGA S A; FROLOV I

PATENT ASSIGNEE: CHIRON CORP; UNIV WASHINGTON

PATENT INFO: US 6465634 15 Oct 2002

APPLICATION INFO: US 1999-415900 8 Oct 1999

PRIORITY INFO: US 1999-415900 8 Oct 1999; US 1996-628594 5 Apr 1996

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2003-147073 [14]

ABSTRACT: DERWENT ABSTRACT:
NOVELTY - A eukaryotic layered vector initiation system (I), comprising a nucleic acid sequence (S) encoding all four alphaviral nonstructural proteins and including an altered sequence (AS) encoding for nonstructural protein 2, such that

when AS is operably incorporated into an RNA vector replicon, the time required to reach 50% inhibition of cellular macromolecular synthesis in cells is increased, is new.

DETAILED DESCRIPTION - A eukaryotic layered vector initiation system (I), comprises a 5' promoter which directs synthesis of alphavirus RNA in vivo from cDNA, a 5' sequence which directs transcription of alphavirus RNA, a nucleic acid sequence which operably encodes all four alphaviral nonstructural proteins, an alphavirus RNA polymerase recognition sequence, and a 3' polyadenylate tract, where the nucleic acid sequence which operably encodes all four alphaviral nonstructural proteins further comprises an altered nucleic acid sequence encoding for nonstructural protein 2 (nsP2) such that when the altered nucleic acid sequence is operably incorporated into an RNA vector replicon, the time required to reach 50 % inhibition of host-cell directed macromolecular synthesis following expression in mammalian cells is increased, as compared to an RNA vector replicon having a wild-type alphavirus nsP2.

WIDER DISCLOSURE - (1) an isolated nucleic acid molecule comprising an altered alphavirus nonstructural protein gene, which when operably incorporated into an recombinant alphavirus, increases the time required to reach 50 % inhibition of host-cell directed macromolecular synthesis following expression in mammalian cells as compared to a wild-type alphavirus; (2) an expression vector comprising a promoter operably linked to the above mentioned nucleic acid molecule; (3) an alphavirus vector construct; (4) an RNA vector replicon capable of translation in a eukaryotic system; (5) recombinant alphavirus particles comprising one or more alphavirus structural proteins, a lipid envelope and an RNA vector replicon; (6) selecting alphavirus or recombinant alphavirus vector variants; (7) togavirus capsid particles that contain substantially no genomic or RNA vector replicon nucleic acids; (8) inducible promoters comprising a core RNA polymerase promoter sequence, an operably linked nucleic acid sequence that directs the DNA binding of the protein that activates transcription from the core promoter sequence, and an operably linked nucleic acid sequence that directs the DNA binding of a protein that represses transcription from the core promoter sequence; (9) an alphavirus structural protein expression cassette; (10) an alphavirus packaging cell line; (11) a host cell containing (I); (12) a pharmaceutical composition comprising (I); (13) a method for making recombinant alphavirus particles; (14) an alphavirus vaccine comprising alphavirus vector constructs, RNA vector replicons, recombinant alphavirus particles or (I); (15) recombinant chimeric togavirus particles; and (16) gene delivery vehicles which produce ribozymes upon intection of a host cell.

BIOTECHNOLOGY - Preferred System: (I) further comprises an alphavirus junction region promoter sequence, a heterologous nucleic acid sequence encoding an interferon, a growth factor (preferably a basic fibroblast growth factor (FGF), platelet-derived growth factor (PDGF) or bone morphogenetic protein), an antigen from a pathogenic agent, preferably a virus (such as hepatitis B virus (HBV), hepatitis C virus (HCV) or human immunodeficiency virus (HIV)), or a lymphokine such as interleukin-2 (IL-2). The 5' promoter which directs synthesis of alphavirus RNA in vivo from cDNA is a eukaryotic promoter, preferably a RNA polymerase II (pol II) promoter, where the pol II promoter is a cytomegalovirus (CMV) or Rous sarcoma virus (RSV) promoter. The sequence encoding the altered nonstructural protein has a

mutation within a L-Xaa-PGG motif, where the mutation is 1-3 amino acids upstream or downstream of the motif. The alphavirus is Sindbis virus, S.A.AR86 virus, Semliki Forest virus, **Venezuelan equine encephalitis virus** or Ross River virus, and the altered nsP2 has a mutation at amino acid residue 726.

ACTIVITY - None given.

MECHANISM OF ACTION - Stimulator of immune response; Gene therapy. No biological data is given.

USE - (I) is useful for stimulating an immune response within a vertebrate, for protein expression and gene therapy.

ADVANTAGE - (I) exhibits reduced, delayed or no inhibition of cellular macromolecular synthesis, thus permitting its use for protein expression and gene therapy, with reduced, delayed, or no development of cytopathic effects or **cell death**.

EXAMPLE - No relevant example is given.(161 pages)

CLASSIFICATION: THERAPEUTICS, Gene Therapy; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; PHARMACEUTICALS, Vaccines

CONTROLLED TERMS: RECOMBINANT ALPHA VIRUS VECTOR-MEDIATED GENE TRANSFER EXPRESSION IN EUKARYOTIC CELL, VIRUS NON-STRUCTURAL PROTEIN, RNA-POLYMERASE RECOGNITION SEQUENCE, INDUCIBLE PROMOTER, TOGA VIRUS CAPSID PARTICLE, LIPID ENVELOP, PACKAGING CELL CULTURE, RIBOZYME, BASIC FIBROBLAST GROWTH FACTOR, PLATELET-DERIVED GROWTH FACTOR, BONE MORPHOGENETIC PROTEIN, APPL. PROTEIN EXPRESSION, NUCLEIC ACID VACCINE, GENE THERAPY RNA ENZYME PROTEIN (22, 13)

L3 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:965027 CAPLUS

DOCUMENT NUMBER: 138:35038

TITLE: Crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug screening

INVENTOR(S): Watowich, Stanley J.; Weaver, Scott C.; Davey, Robert A.

PATENT ASSIGNEE(S): Board of Regents, the University of Texas System, USA

SOURCE: U.S. Pat. Appl. Publ., 25 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:
MAIN: C12N009-64
SECONDARY: C12P021-02; C12N005-06; C12N009-20

US PATENT CLASSIF.: 435226000; 435069100; 435320100; 435325000; 435198000

CLASSIFICATION: 6-3 (General Biochemistry)
Section cross-reference(s): 1, 3, 4, 10, 75

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002192799	A1	20021219	US 2001-981286	20011015

PRIORITY APPLN. INFO.: US 2000-240187P P 20001013

ABSTRACT:
The present invention provides collections of polypeptides constructed using combinatorial libraries, where each polypeptide includes a region Xaan, wherein n is from about 5 to about 21, and each Xaa is independently a random amino acid. Each polypeptide includes a fragment of the **Venezuelan** ***equine*** **encephalitis virus** (VEEV) capsid protein C-terminal domain (CCD, residues 119-275). Polynucleotides encoding the polypeptides, are also provided, as are methods for identifying a polypeptide

within a collection that prevents **cell death** after exposure to a pathogen or a toxin, and methods for identifying a polypeptide within a collection that binds a pathogen, a toxin, a polypeptide, or a polynucleotide. The present invention also provides methods for crystg. a polypeptide. Crystn. and crystal structure of the VEEV CCD is disclosed. Cloning combinatorial adaptein libraries into packaging vectors is presented. This describes the insertion of a DNA oligonucleotide, which contains a stretch of random sequence, into the DNA sequence coding for the tat-CCD fusion protein, within a retrovirus packaging vector. This allows for the expression of a fusion protein that contains tat, CCD, and a random peptide inserted into the CCD sequence. The assays to identify the adapteins that protect cells and animals from RVFV are described. The ability of purified recombinant Tat-CCD carrier protein to cross cell membranes was examd.

SUPPL. TERM: VEEV capsid protein crystn crystal structure drug discovery screening; adaptein combinatorial library VEEV capsid protein drug discovery screening

INDEX TERM: Fusion proteins (chimeric proteins)
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(adaptein; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Fusion proteins (chimeric proteins)
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(capsid protein with cell peremeant peptide and Tat; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); USES (Uses)
(capsid; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Rift Valley fever virus
(challenge of adaptein library-contg. cells with RVFV; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Genetic vectors
Molecular cloning
Murine leukemia virus
PCR (polymerase chain reaction)
Retroviral vectors
(cloning combinatorial adaptein libraries into packaging vectors; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Primers (nucleic acid)
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(cloning combinatorial adaptein libraries into packaging vectors; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Crystal growth
Crystal morphology
Crystal structure
Drug screening
Peptide library
Venezuelan equine encephalitis virus
(crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Polyoxyalkylenes, uses
ROLE: NUU (Other use, unclassified); USES (Uses)
(crystn. soln. contg.; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: DNA sequences
(for capsid protein and adapteins; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Protein sequences
(of capsid protein and adapteins; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Virus
(pathogenic, screening for polypeptide preventing **cell death** after exposure to pathogen or toxin; crystal structure of VEEV capsid protein C-terminal domain, and cloning combinatorial adaptein libraries into packaging vectors)

INDEX TERM: Biological transport
(permeation, of recombinant Tat-CCD carrier protein through cell membrane; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: **Cell death**
Pathogen
Pathogenic bacteria
Rickettsia
(screening for polypeptide preventing **cell death** after exposure to pathogen or toxin; crystal structure of VEEV capsid protein C-terminal domain, and cloning combinatorial adaptein libraries into packaging vectors)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(screening for polypeptide preventing **cell death** after exposure to pathogen or toxin; crystal structure of VEEV capsid protein C-terminal domain, and cloning combinatorial adaptein libraries into packaging vectors)

INDEX TERM: Antibacterial agents
Antimicrobial agents
Antiviral agents
Fungicides

(screening for; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Antitoxins
ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(screening for; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Transcription factors
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(tat, fusion products with capsid protein and cell peremeant peptide; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: Fungi
(zoopathogenic, screening for polypeptide preventing **cell death** after exposure to pathogen or toxin; crystal structure of VEEV capsid protein C-terminal domain, and cloning combinatorial adaptein libraries into packaging vectors)

INDEX TERM: 478749-39-2DP, subfragments and variants are claimed
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(amino acid sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: 478749-43-8P
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(amino acid sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: 478749-41-6P
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(amion acid sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: 188842-14-0P 189036-91-7P 191936-91-1P 478314-83-9P
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(cell peremeant region; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: 57-13-6, Urea, uses 7783-20-2, Ammonium sulfate, uses 7786-30-3, Magnesium chloride, uses 25322-68-3, Polyethylene glycol
ROLE: NUU (Other use, unclassified); USES (Uses)
(crystn. soln. contg.; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: 478749-40-5P
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(nucleotide sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: 478749-42-7P
ROLE: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(nucleotide sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: 478749-38-1
ROLE: BSU (Biological study, unclassified); BUU (Biological use, unclassified); CST (Combinatorial study, unclassified); PRP (Properties); BIOL (Biological study); CMBI (Combinatorial study); USES (Uses)
(nucleotide sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug screening)

INDEX TERM: 478750-94-6 478750-95-7 478750-96-8 478750-97-9
478750-98-0 478750-99-1 478751-00-7 478751-01-8
478751-02-9 478751-03-0 478751-04-1 478751-05-2
478751-06-3 478751-07-4 478751-08-5 478751-09-6
478751-10-9
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug screening)

INDEX TERM: 478751-11-0
ROLE: PRP (Properties)
(unclaimed protein sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug screening)

INDEX TERM: 478751-12-1 478751-13-2
ROLE: PRP (Properties)
(unclaimed sequence; crystal structure of VEEV capsid protein C-terminal domain, cloning combinatorial adaptein libraries into packaging vectors and applications to drug discovery and drug screening)

L3 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:798403 CAPLUS
DOCUMENT NUMBER: 135:353692
TITLE: Methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection
INVENTOR(S): Dubensky, Thomas W., Jr.; Polo, John M.; Perri, Silvia; Belli, Barbara A.
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C12N007-00
SECONDARY: C12N007-01; C12N007-04
CLASSIFICATION: 3-1 (Biochemical Genetics)
Section cross-reference(s): 10
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081553	A1	20011101	WO 2001-US13255	20010425

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: US 2000-199579P P 20000425

ABSTRACT:
The invention provides host cell tolerant alphavirus-based vectors, which include an alphavirus replicon particle, eukaryotic layered vector initiation system, alphavirus vector construct or RNA vector replicon, for protein expression and gene delivery with reduced, delayed, or no development of cytopathic effect CPE or **cell death**. In particular, the invention discloses that an alphavirus nonstructural protein 2 gene, when operably incorporated into the vectors, exhibits a noncytopathic phenotype or confers the ability to establish persistent replication. The invention further provides stably transformed cell lines with the vectors as well as methods of using such replicons, constructs, particles and eukaryotic layered vector initiation systems for expression of recombinant proteins.

SUPPL. TERM: alphavirus RNA replicon vector persistent infection
INDEX TERM: Proteins, specific or class
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(NS2 (nonstructural, 2), gene for; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)
INDEX TERM: Alphavirus
(S.A. AR86; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)
INDEX TERM: Eukaryote (Eukaryotae)
(as host cell; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)
INDEX TERM: RNA viruses
(as viral vectors; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)
INDEX TERM: Insect (Insecta)
Vertebrate (Vertebrata)
(cell, as host; methods of constructing host cell tolerant alphavirus-based expression vectors for

persistent infection)

INDEX TERM: Proteins, specific or class
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(coat, R17, temp. sensitive, expressed by alphavirus vector; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Virion structure
(envelope, alphavirus replicon particle comprising; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Genetic vectors
(eukaryotic layered; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Promoter (genetic element)
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(for expressing foreign protein; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Animal cell line
(for packaging RNA virus; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Virus vectors
(for persistent infection; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Animal cell
(mammalian, as host cell; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Genetic engineering
Ross River virus
Semliki Forest virus
Sindbis virus
Venezuelan equine encephalitis virus
(methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Transgene
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Replicon
(of alphavirus; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Mutagenesis
(site-directed, substitution, of nsP2; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: Proteins, specific or class
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(structural, viral vector contg.; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: 11096-26-7, Erythropoietin 106096-93-9, Basic FGF
113189-02-9, Factor VIII 127464-60-2, Vascular endothelial growth factor
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(expressed by alphavirus vector; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: 105913-11-9, Plasminogen activator
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(t-PA, expressed by alphavirus vector; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: 222659-33-8 371798-57-1 371798-58-2 371798-59-3
371798-60-6 371798-61-7 371798-62-8 371798-63-9
371798-64-0 371798-65-1 371798-66-2 371798-67-3
371798-68-4 371798-69-5 371798-70-8 371798-71-9
371798-72-0 371798-73-1 371798-74-2 371798-75-3
371798-76-4 371798-77-5 371798-78-6 371798-79-7
371798-80-0 371798-81-1 371798-82-2 371798-83-3
371798-84-4 371798-85-5 371798-86-6 371798-87-7
371798-88-8 371798-89-9 371798-90-2 371798-91-3
371798-92-4 371798-93-5
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

INDEX TERM: 371966-59-5 371966-60-8 371966-61-9 371966-62-0
371966-63-1 371966-65-3 371966-66-4
ROLE: PRP (Properties)
(unclaimed sequence; methods of constructing host cell tolerant alphavirus-based expression vectors for persistent infection)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Johnston; US 5792462 A 1998 CAPLUS

L3 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:747832 CAPLUS

DOCUMENT NUMBER: 135:313607

TITLE: Fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy

INVENTOR(S): Vile, Richard G.; Harrington, Kevin; Murphy, Stephen; Bateman, Andrew

PATENT ASSIGNEE(S): Mayo Foundation for Medical Education and Research, USA

SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:
MAIN: C07K014-08

CLASSIFICATION: 1-6 (Pharmacology)
Section cross-reference(s): 3

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074861	A2	20011011	WO 2001-US10250	20010330
WO 2001074861	A3	20020314		
WO 2001074861	C2	20021227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002150556 A1 20021017 US 2001-822634 20010330
PRIORITY APPLN. INFO.: US 2000-193977P P 20000331

ABSTRACT:
A method of ensuring tumor specific expression of a cytotoxic gene is described. Th preferred gene encodes a viral fusogenic peptide that stimulates syncytium formation. The gene is under control of a tumor-specific promoter and is flanked by a pair of sites recognized by a site-specific recombinase. The recombinase gene is under control of a promoter that functions in normal tissue, but not in the tumor cell. In normal tissues, the fusogenic protein gene is excised by site-specific recombination and lost. In tumor cells, the gene is not lost by excision and is expressed. After cell fusion and syncytium formation, the tumor cells die.

SUPPL. TERM: fusogenic glycoprotein tumor cell fusion death; recombinase regulation fusogenic protein gene expression tumor cell; syncytium formation cancer therapy

INDEX TERM: Enzymes, biological studies
ROLE: BUU (Biological use, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(DNA-recombining, cre; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Enzymes, biological studies
ROLE: BUU (Biological use, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(DNA-recombining, gene FLP; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Enzymes, biological studies
ROLE: BUU (Biological use, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(DNA-recombining; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Proteins, specific or class
ROLE: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)
(F, fusogenic; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(F1, as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(F2, as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse);

BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G, as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HN (hemagglutinin-neuraminidase), as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Envelope proteins
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Gene, animal
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(c-erbB2, tumor-specific promoter; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: **Cell death**
(**cell** fusion induced, in tumors; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Macrophage
(cell fusions between tumor cells and; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Canine distemper virus
Measles virus
Simian parainfluenza virus 5
(fusion protein of; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Bovine herpesvirus
Cercopithecine herpesvirus 9
Friend murine leukemia virus
Herpes virus B
Human herpesvirus
Human herpesvirus 1
Human herpesvirus 3
Human immunodeficiency virus 1
Human parainfluenza virus 3
Influenza virus
Mason-Pfizer monkey virus
Mumps virus
Newcastle disease virus
Russian spring summer encephalitis virus
Simian parainfluenza virus 41
Venezuelan equine encephalitis virus
West Nile virus
(fusogenic proteins of; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Avian infectious bronchitis virus
Bovine coronavirus
Mokola virus
Murine hepatitis virus
Porcine respiratory virus

Rabies virus
Togaviridae
Vesicular stomatitis virus
(fusogenic spike glycoprotein of; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); THU (Therapeutic use); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process); USES (Uses)
(fusogenic; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gB, as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gH, as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Cytokines
Interleukin 1
Interleukin 12
Interleukin 2
Interleukin 3
Interleukin 4
Interleukin 5
Interleukin 6
Interleukin 7
Tumor necrosis factors
ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene for, tumor-specific expression for; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Gene, microbial
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(gin, regulated expression of; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Genetic element
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hypoxia response element HRE, in expression constructs for fusogenic protein genes; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Gene, microbial
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(pin, regulated expression of; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Recombination, genetic
(site-specific excisive, tissue-specific, of recombinase genes; fusogenic protein genes regulated by

tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spike, G, as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Glycoproteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spike, as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Cell fusion
(stimulation of, in tumors; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Proteins, specific or class
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(surface projection, as fusogenic glycoprotein; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Carcinoembryonic antigen
Myelin basic protein
.alpha.-Fetoproteins
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-specific promoter of gene for; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Promoter (genetic element)
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor-specific, expression of fusogenic protein gene from; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: Interferons
ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(.gamma., gene for, tumor-specific expression for; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: 52350-85-3, Integrase
ROLE: BUU (Biological use, unclassified); CAT (Catalyst use); BIOL (Biological study); USES (Uses)
(bacteriophage .lambda.; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: 9002-06-6, Thymidine kinase 9025-05-2, Cytosine deaminase 9037-41-6, Nitroreductase
ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene for, as suicide gene for tumor cells; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

INDEX TERM: 83869-56-1, GM-CSF
ROLE: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene for, tumor-specific expression for; fusogenic protein genes regulated by tissue-specific excision and

their use in cancer therapy)
INDEX TERM: 9002-10-2, Tyrosinase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(tumor-specific promoter of gene for; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)
INDEX TERM: 217877-36-6 337445-68-8, GenBank AR163174 337445-69-9, GenBank AR163175 337445-76-8, GenBank AR124531 337445-77-9, GenBank AR163183 337445-78-0, GenBank AR163184 337445-79-1, GenBank AR163185 366376-44-5, GenBank AX269135 366376-45-6, GenBank AX269136 366376-46-7, GenBank AX269141 366376-47-8, GenBank AX269142 366376-48-9, GenBank AX269143 366376-49-0, GenBank AX269144 366376-50-3, GenBank AX269145 366376-51-4, GenBank AX269146 366521-55-3, 2: PN: WO0174861 SEQID: 2 unclaimed DNA 366521-56-4 367317-49-5, 1: PN: WO0174861 SEQID: 1 unclaimed DNA
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; fusogenic protein genes regulated by tissue-specific excision and their use in cancer therapy)

L3 ANSWER 7 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97107643 EMBASE
DOCUMENT NUMBER: 1997107643
TITLE: Apoptotic **cell death** is an important cause of neuronal injury in experimental **Venezuelan equine encephalitis virus** infection of mice.
AUTHOR: Jackson A.C.; Rossiter J.P.
CORPORATE SOURCE: A.C. Jackson, Department of Medicine, Queen's University, 78 Barrie Street, Kingston, Ont. K7L 3J7, Canada. jacksona@post.queensu.ca
SOURCE: Acta Neuropathologica, (1997) 93/4 (349-353).
Refs: 17
ISSN: 0001-6322 CODEN: ANPTAL
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
Mice develop a fatal encephalomyelitis after infection with the Trinidad donkey strain of Venezuelan equine encephalitis (**VEE**) virus. Adult mice were inoculated intraperitoneally with **VEE** virus and the brains were examined at different time points. Morphological changes were assessed by histological staining. **VEE** virus antigen was detected with immunoperoxidase staining, and DNA fragmentation was evaluated in situ using the terminal deoxynucleotidyl transferase-mediated dUTP-digoxigenin nick end labeling (TUNEL) method. **VEE** antigen was found in many areas of the brain and it was prominent in neurons. There were mild associated inflammatory changes. DNA fragmentation was demonstrated in many of these areas using TUNEL. In areas with TUNEL staining, morphological neuronal changes ranged from nuclear chromatin condensations to nuclear and cellular fragmentation, which are characteristic of apoptosis. There is strong morphological and biochemical evidence of apoptotic **cell death** in this experimental model of **VEE** virus infection.

CONTROLLED TERM: Medical Descriptors:
*apoptosis
*encephalitis: ET, etiology

*nerve cell lesion: ET, etiology
*venezuelan equine encephalomyelitis alphavirus
animal experiment
animal model
animal tissue
article
cell death
dna determination
experimental infection
histology
immunoperoxidase staining
mouse
neuropathology
nonhuman
priority journal
Drug Descriptors:
dna fragment: EC, endogenous compound

L3 ANSWER 8 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 77137087 EMBASE
DOCUMENT NUMBER: 1977137087
TITLE: Lymphoreticular and myeloid pathogenesis of Venezuelan equine encephalitis in hamsters.
AUTHOR: Walker D.H.; Harrison A.; Murphy K.; et al.
CORPORATE SOURCE: Cent. Dis. Contr., PHS, USDHEW, Atlanta, Ga., United States
SOURCE: American Journal of Pathology, (1976) 84/2 (351-370).
CODEN: AJPAA4
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
025 Hematology
LANGUAGE: English
ABSTRACT:
Ultrastructural, histopathologic, and virologic studies of adult hamsters infected with virulent Venezuelan equine encephalomyelitis (**VEE**) virus (Subtype I B) demonstrated precise chronologic and topographic progression of lesions and viral replication in extraneural sites. Thymus contained the earliest lesions and the highest initial and subsequent viral titers. No particular cytotropism was observed as highly efficient viral replication and severe cytonecrosis proceeded. Early cortical necrosis of splenic periarteriolar lymphocytic sheath was followed by lymphoblastoid repopulation of the peripheral zone. Massive bone marrow necrosis was accompanied by ultrastructural evidence of **VEE** viral particle production in reticulum cells, rubricytes, myeloid cells, lymphoblastoid cells, and megakaryocytes. Speed, efficiency, destructiveness, and relative sensitivity of virtually all lymphoreticular and hematopoietic cells were hallmarks of virulent **VEE** infection in the hamster.

CONTROLLED TERM: Medical Descriptors:
*bone marrow cell
***cell death**
*spleen cell
*thymocyte
*venezuelan equine encephalomyelitis alphavirus
*virus infection
electron microscopy
autopsy
in vitro study
microorganism
theoretical study
histology

L3 ANSWER 9 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 76200154 EMBASE
DOCUMENT NUMBER: 1976200154

TITLE: Morphological changes in the pancreas of the hamster during Venezuelan equine encephalomyelitis (**VEE**) virus infection.
AUTHOR: Rodriguez G.
CORPORATE SOURCE: Lab. Nac. Salud, INPES, Bogota, Colombia
SOURCE: Patologia, (1975) 13/3 (297-310).
CODEN: PTOLAT
DOCUMENT TYPE: Journal
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
047 Virology
048 Gastroenterology
LANGUAGE: English
ABSTRACT:
Twelve hamsters inoculated intraperitoneally with a colombian strain of ***VEE*** virus (Group I D), suffered necrotic damage of the pancreatic acini. Viral development implied an increase in the size of the Golgi apparatus, presence of perigolgian masses of viroplasm and complex membranes in whose relation, as well as budding from the cell membrane mature viruse are formed. The zymogen granules became elongated, pyriform, thinner and of different sizes. Virus particles are frequently seen within the acinar lumen, thus being probably conveyed to the duodenum. Numerous pyriform vesicles with a small central dot are often connected to the plasma membrane. Viral particles are seen within the capillary lumina, budding from the luminal side of endothelial cells, or being trapped within pynocitic vesicles.

CONTROLLED TERM: Medical Descriptors:
*capillary
*cell granule
***cell death**
*cytoplasm vesicle
*endothelium cell
*acinar cell
*pancreas islet beta cell
*pancreas necrosis
*pinocytosis
*venezuelan equine encephalomyelitis alphavirus
*virus infection
*virus particle
*virus replication
theoretical study
microorganism
diagnosis
histology
electron microscopy
Drug Descriptors:
*zymogen granule

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	35.79	36.00

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=> s inhibitor or drug
             0 INHIBITOR
            32 DRUG
L4          32 INHIBITOR OR DRUG

=> d his

     (FILE 'HOME' ENTERED AT 12:51:36 ON 12 MAY 2003)

     FILE 'MEDLINE, BIOSIS, BIOTECHDS, CAPLUS, EMBASE' ENTERED AT 12:51:44 ON
     12 MAY 2003
L1          2090 S (VENEZUELAN EQUINE ENCEPHALITIS VIRUS) OR VEE
L2        168238 S CELL (A) DEATH
L3             9 S L1 AND L2

     FILE 'STNGUIDE' ENTERED AT 12:55:12 ON 12 MAY 2003
L4            32 S INHIBITOR OR DRUG

=> file .biotech
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.36      36.36

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                         ENTRY    SESSION
CA SUBSCRIBER PRICE                                       0.00      -1.95

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     (FILE 'HOME' ENTERED AT 12:51:36 ON 12 MAY 2003)

     FILE 'MEDLINE, BIOSIS, BIOTECHDS, CAPLUS, EMBASE' ENTERED AT 12:51:44 ON
     12 MAY 2003
L1          2090 S (VENEZUELAN EQUINE ENCEPHALITIS VIRUS) OR VEE
L2        168238 S CELL (A) DEATH
L3             9 S L1 AND L2

     FILE 'STNGUIDE' ENTERED AT 12:55:12 ON 12 MAY 2003
L4            32 S INHIBITOR OR DRUG

     FILE 'MEDLINE, BIOSIS, BIOTECHDS, CAPLUS, EMBASE' ENTERED AT 12:58:58 ON
     12 MAY 2003

=> s inhibitor or drug and apoptosis
L5       1312299 INHIBITOR OR DRUG AND APOPTOSIS

=> s l3 and l5
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L6 0 L3 AND L5

=> l3 and inhibitor
L3 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l3 and inhibitor
L7 0 L3 AND INHIBITOR

=> s (inhibitor or drug) and apoptosis
L8 101757 (INHIBITOR OR DRUG) AND APOPTOSIS

=> s drug screening
L9 103106 DRUG SCREENING

=> s l8 and l9
L10 2198 L8 AND L9

=> s VEE
L11 1493 VEE

=> s l10 and l11
L12 0 L10 AND L11

=> s inhibitor
L13 1256865 INHIBITOR

=> s l11 and l13
L14 4 L11 AND L13

=> d iall l14 1-4

L14 ANSWER 1 OF 4 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-09805 BIOTECHDS
TITLE: Composition useful for treating or preventing HIV infections, comprises two or more isolated nucleic acids encoding env, gag or pol gene product of HIV or immunogenic fragment of the gene products;
vaccine composition having virus-like particle inhibition, integrase-**inhibitor**, RNA-ase-H-**inhibitor** and reverse-transcriptase-**inhibitor** activity, useful for virus infection gene therapy
AUTHOR: OLMSTED R; KEITH P; DRYGA S; CALEY I; MAUGHAN M; JOHNSTON R; DAVIS N; SWANSTROM R
PATENT ASSIGNEE: ALPHAVAX INC; UNIV NORTH CAROLINA
PATENT INFO: WO 2002003917 17 Jan 2002
APPLICATION INFO: WO 2000-US21701 7 Jul 2000
PRIORITY INFO: US 2000-216995 7 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-171664 [22]
ABSTRACT: DERWENT ABSTRACT:
NOVELTY - A composition (I) comprising isolated nucleic acids (II) encoding env, gag or pol gene product of human immunodeficiency virus or immunogenic fragment of the gene products, is new. The gag gene product is modified to inhibit formation of virus-like particles containing gag gene product and their release from cells, and the pol gene product is modified to inhibit reverse transcriptase activity.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a composition (III) comprising a population of alpha-virus replicon particles

(IV) or a population of alpha-virus replicon virosomes (V) comprising (II), where the nucleic acids are each contained within a separate alpha-virus replicon particle or virosome; (2) making (M1) (IV) by: (a) providing a first, second or third helper cell for producing a first, second or third population of infectious replication defective alpha-virus particles, comprising in a alpha-virus-permissive cell: (i) an alpha-virus replicon RNA, wherein the replicon RNA comprises an alpha-virus packaging signal (II) and the replicon RNA lacks sequence encoding alpha-virus structural proteins; (ii) a first helper RNA separate from the replicon RNA, where the first helper RNA encodes at least one alpha-virus structural protein and does not encode at least one other alpha-virus structural protein; and (iii) one or more additional helper RNAs separate from the replicon RNA and separate from the first helper RNA, where the additional helper RNAs encodes at least one other alpha-virus structural protein not encoded by the first helper RNA, and where at least one of the helper RNA is lacking an alpha-virus packaging signal, where the combined expression of the alpha-virus replicon RNA and the helper RNAs produces an assembled alpha-virus particle which is able to infect a cell and is unable to complete viral replication, and the first; second or third population contains no detectable replication-competent alpha-virus particles as determined by passage on permissive cells in culture; (b) producing the alpha-virus particles in the helper cell, and collecting the alpha-virus particles from the helper cells; and (c) combining the first, second and third population of alpha-virus particles produced from the first, second and third helper cells, respectively, thus producing (IV); (3) a population of alpha-virus replicon particles produced by M1; (4) producing (M2) (V), by producing a first, second and third population of alpha-virus replicon virosomes by combining alpha-virus replicon RNA comprising (II), alpha-virus glycoproteins E1 and E2, non-cationic lipids and detergent, gradually removing detergent, where alpha-virus replicon virosomes are produced, and combining the first, second and third population of alpha-virus replicon virosomes to produce (V); (5) an alpha-virus replicon virosome (VI) comprising an alpha-virus replicon RNA encapsulated by a lipid bilayer comprising alpha-virus glycoproteins, E1 and E2; (6) producing (M3) (VI); (7) an alpha-virus replicon virosome produced by M3; (8) a composition (VII) comprising heparin affinity-purified alpha-virus replicon particles (VIII) which comprises at least one structural protein comprising one or more attenuating mutations; (9) preparing (M4) (VIII); (10) a composition produced by M4; (11) producing (M5) an alpha-virus replicon particle (VRP) for use in vaccine; (12) VRP (IX) produced by M5; (13) an isolated nucleic acid (X) encoding a pol gene product of HIV or its immunogenic fragment, where the pol gene produce comprises the modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptase functions in the pol gene product; (14) a composition (XI) comprising (X); (15) a vector (XII) comprising (X); (16) a cell (XIII) comprising (XII); (17) an alpha-virus replicon particle (XIV) comprising (X); (18) production (M6) of (XIV), comprising culturing (XIII); and (19) an alpha-virus replicon particle produced by M6.

BIOTECHNOLOGY - Preferred Composition: In (III), the alpha-virus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. The pol gene product comprises a

modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptional functions in the pol gene product. Preferred Method: In M1, the replicon RNA, the first helper RNA, and one or more additional helper RNAs comprises one or more attenuating mutations. The alpha-virus replicon RNA of at least one of the first, second and third helper cell comprises a sequence encoding at least one alpha-virus structural coating, where the first helper RNA and one or more additional helper RNAs in the first, second, and third helper cell, encodes at least one other alpha-virus structural coatings not encoded by the replicon RNA. Preferred Virosome: In (VI), the alpha-virus glycoproteins are Venezuelan Equine Encephalitis glycoproteins E1 and E2.

ACTIVITY - Anti-HIV (human immunodeficiency virus).

MECHANISM OF ACTION - Vaccine; inducer of immune response (claimed). Immunological response of mice to alpha-virus replicon particles (VRP)-gag vaccine was tested: Mice were injected subcutaneously in two doses, with 8-9 mice in each group. The mice were immunized once, then immunized a second time, with the same dose, 28 days later. Serum was collected the day prior to the first immunization, then at day 27 (after 1st immunization) and at day 35 (after 2nd immunization). The mice showed a vigorous, antigen-specific humoral response to HIV-1 Clade C VRP-gag vaccine.

USE - (I), (III), (IV), (VI) or (XI) is useful for inducing an immune response to human immunodeficiency virus (HIV) or for treating or preventing HIV infection in a subject. (IX) is useful in a vaccine. (All claimed). (I) or (III) is useful for administering a protein or peptide to a subject. (VII) is useful as a clinical trial material and commercial product.

ADMINISTRATION - (III) is administered by parenteral (e.g. subcutaneous, intradermal, intramuscular, intravenous, intraarticular) or intranasal route at a dose of 10 to the power 3-10 to the power 7, preferably 10 to the power 4-10 to the power 6 alpha-virus replicon particles.

ADVANTAGE - (VI) is easy to prepare, stable, and pure, since it is devoid of any cellular components being made in a cell free system.

EXAMPLE - Replicon particles for use as a vaccine were produced using the Venezuelan Equine Encephalitis virus (**VEE**)-based vector system, originally developed from a full-length, infectious cDNA clone of the RNA genome of **VEE**. One or more attenuating mutations were inserted into the clone to generate attenuated **VEE** vaccine vectors. The constructs were genetically modified to create an RNA replicon, and one or more helper RNAs to allow packaging. The replicon RNA expressed an HIV gene, e.g. the Clade C HIV-1 gag gene. The replicon RNA was packaged into virus-like particles (virus replicon particles or VRPs) that were infectious for only one cycle. During this cycle, the characteristics of the alpha-virus-based vector resulted in very high levels of expression of the replicon RNA in cells to which the VRP was targeted. In the cytoplasm of the target cell, the replicon RNA was first translated to produce viral replicase proteins necessary to initiate self-amplification and expression. The HIV-1 Clade C gag gene was encoded by a subgenomic mRNA, abundantly transcribed from a negative-sense replicon RNA intermediate, leading to high-level expression of HIV-1 Clade C gag product. Since the **VEE** structural protein genes were not encoded by the replicon RNA, progeny virion particles were not assembled, thus limiting to a single cycle within the infected target cell.

Only the replicon RNA was packaged into VRPs, as the helper RNAs lacked the cis-acting packaging sequence required for encapsidation. The split helper or bipartite system greatly reduced the chance for an intact genome being assembled by recombination, and as a back-up safety feature, one or more highly attenuating mutations, such as those contained in the glycoprotein genes in V3014 were incorporated. Overall, the design of the VRPs incorporated several layered and redundant safety features. In addition to the above-described split helper system and attenuating mutations, over one-third of the genome of the virus was removed, creating a defective genome which prevented spread from the initially infected target cell. If a statistically rare recombination event occurred to yield replication competent virus (RCV), the resulting virus was a highly attenuated **VEE** strain.(201 pages)

CLASSIFICATION: PHARMACEUTICALS, Vaccines; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; DISEASE, HIV and Other Virus Infections; THERAPEUTICS, Gene Therapy

CONTROLLED TERMS: COMPOSITION CHARACTERIZATION, HIV VIRUS MUTANT ENV, GAG, POL GENE, VENEZUELAN-HORSE-ENCEPHALITIS VIRUS VECTOR, HOST CELL INFECTION, ALPHA VIRUS GLYCOPROTEIN, VIRUS-LIKE PARTICLE INHIBITION, INTEGRASE-**INHIBITOR**,RNA-ASE-H-**INHIBITOR**, REVERSE-TRANSCRIPTASE-**INHIBITOR** ACT., APPL. VIRUS INFECTION THERAPY, GENE THERAPY, NUCLEIC ACID VACCINE, RECOMBINANT VACCINE, CLINICAL TRIAL LEUKO VIRUS RETRO VIRUS AIDS LENTI VIRUS ARBO VIRUS ENZYME-**INHIBITOR** IMMUNOSTIMULANT (21, 32)

L14 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1992:531480 CAPLUS

DOCUMENT NUMBER: 117:131480

TITLE: Synthesis and antiviral evaluation of N-carboxamidine-substituted analogs of 1-.beta.-D-ribofuranosyl-1,2,4-triazole-3-carboxamidine hydrochloride.

AUTHOR(S): Gabrielsen, Bjarne; Phelan, Michael J.; Barthel-Rosa, Luis; See, Cathy; Huggins, John W.; Kefauver, Deborah F.; Monath, Thomas P.; Ussery, Michael A.; Chmurny, Gwendolyn N.; et al.

CORPORATE SOURCE: U.S. Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21702, USA

SOURCE: Journal of Medicinal Chemistry (1992), 35(17), 3231-8
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 33-9 (Carbohydrates)
Section cross-reference(s): 1, 34

OTHER SOURCE(S): CASREACT 117:131480

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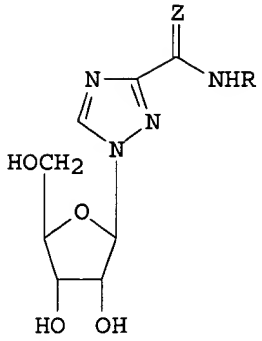

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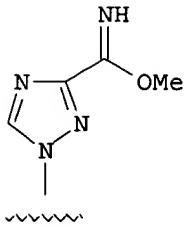

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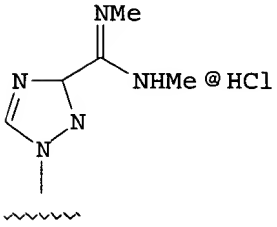

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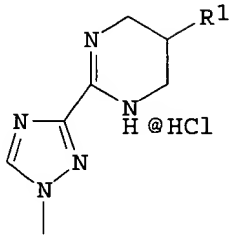

IV

ABSTRACT:
Ten, hitherto unreported, analogs of 1-(.beta.-D-ribofuranosyl)-1,2,4-triazole-3-carboxamidine hydrochloride (I.cntdot.HCl; R = H, Z = NH; ribamidine) and Me carboximidate II were synthesized. These include the N-cyano (I; R = CN, Z = NH), N-alkyl (I; R = Me, Bu, octyl, Z = NH), N-amino acid [I; R = CH2CO2H, CH(CO2H)CH2CONH2, CH(CO2H)CH2CH2CONH2, Z = NH], N,N'-disubstituted III and IV (R1 = H, OH), and the N-methylated carboxamide analogs I (R = Me, Z = O) of ribavirin. In addn., a new facile synthesis of carboxamidine I.cntdot.HCl (R = H, Z = NH) was also developed. All compds. were evaluated for biol. activity against the following RNA viruses: Punta Toro (PT) and sandfly fever (SF) viruses (bunyaviruses); Japanese encephalitis (JE), yellow fever (YF), and dengue-4 viruses (flaviviruses); parainfluenza type 3 (PIV3), respiratory syncytial virus (RSV), and measles viruses (paramyxoviruses); influenza A and influenza B viruses (orthomyxoviruses); Venezuelan equine encephalomyelitis virus (**VEE**, alphavirus); human immunodeficiency virus type-1 (HIV-1, lentivirus); the DNA-contg. vaccinia (VV) virus (poxvirus); and adeno type 5 (Ad5) viruses. All of the compds. except for I (R = CN, Z = NH) and IV exhibited activity against the bunyaviruses such as that obsd. with I.cntdot.HCl (R = H, Z = NH); however, higher IC50 values were generally obsd. Glycine analog I (R = CH2CO2H, Z = NH) showed activity in PT-virus-infected mice in terms of increased survivors and decreased markers of viral pathogenicity. Carboxamidine I.cntdot.HCl (R = H, Z = NH), carboximidate II, and di-Me amidine III exhibited activity against dengue type-4 virus. Monomethyl amidine I.cntdot.HCl (R = Me, Z = NH) demonstrated activity against RSV, PIV/3, and, to a lesser extent, influenza A and B. Activity of I.cntdot.HCl (R = Me, Z = NH) generally required higher IC50 values than unsubstituted I.cntdot.HCl (R = H, Z = NH). The latter exhibited hitherto unreported activity against RSV; therapeutic indexes for I.cntdot.HCl (R = H, Z = NH) against RSV and PIV3 were >64 and >21. No substantial in vitro activity was obsd. for any of the compds. tested against Ad5, measles, JE, YF, ***VEE*** , or HIV-1. In addn., evidence is presented which argues in favor of a distinct antiviral mechanism of action for carboxamidines, e.g. III, in contrast to a role as a carboxamide precursor.

SUPPL. TERM: ribavirin analog synthesis antiviral pathogenicity; triazolecarboxamidine ribofuranoside synthesis antiviral; AIDS **inhibitor** triazolecarboxamidine ribofuranoside; HIV **inhibitor** triazolecarboxamidine ribofuranoside; virucide

triazolecarboxamidine ribofuranoside synthesis; carboxamidine analog ribavirin synthesis antiviral; ribamidine synthesis virucide

INDEX TERM: Acquired immune deficiency syndrome
(inhibitors, ribavirin carboximidate analogs, inactive)

INDEX TERM: Virucides and Virustats
(ribavirin carboximidate analogs)

INDEX TERM: Nucleotides, preparation
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(analogs, ribavirin carboximidate, prepn. and antiviral activity of)

INDEX TERM: Toxicity
(cytotoxicity, of ribavirin carboximidate analogs)

INDEX TERM: Virus, animal
(human immunodeficiency 1, inhibitors, ribavirin carboximidate analogs, inactive)

INDEX TERM: 40371-99-1
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis and imidation of, with ammonium chloride)

INDEX TERM: 36791-04-5DP, Ribavirin, analogs 142633-76-9P 142633-77-0P 142633-78-1P 142633-79-2P 142633-80-5P 142633-81-6P 142633-82-7P 142633-83-8P 142633-84-9P 142633-85-0P 142633-86-1P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antiviral activity of)

INDEX TERM: 40372-00-7P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn., reactions, and antiviral activity of)

INDEX TERM: 120362-25-6
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reactions of, in prepn. of ribavirin carboximidate analogs)

L14 ANSWER 3 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 1999106908 EMBASE

TITLE: Systemic antibiotics: A review and their use in chronic wounds.

AUTHOR: Hernandez R. Jr.

CORPORATE SOURCE: Dr. R. Hernandez Jr., Department of Medicine, Univ. of Miami School of Medicine, Miami, FL, United States

SOURCE: Dermatologic Therapy, (1999) 9/- (44-62).
Refs: 72
ISSN: 1396-0296 CODEN: DETHFE

COUNTRY: Denmark

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
013 Dermatology and Venereology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*wound care
*wound healing
*antimicrobial activity
*wound infection: DR, drug resistance

*wound infection: DT, drug therapy
drug use
antibiotic resistance
drug structure
nausea: SI, side effect
diarrhea: SI, side effect
vomiting: SI, side effect
abdominal pain: SI, side effect
heart ventricle tachycardia: SI, side effect
heart arrest: SI, side effect
drug contraindication
arthropathy: SI, side effect
ototoxicity: SI, side effect
nephrotoxicity: SI, side effect
disease association
insulin dependent diabetes mellitus
immunocompetence
neutropenia
human immunodeficiency virus infection
kidney failure
aging
human
oral drug administration
intramuscular drug administration
intravenous drug administration
topical drug administration
review
Drug Descriptors:
*aminoglycoside: AE, adverse drug reaction
*aminoglycoside: DO, drug dose
*aminoglycoside: IT, drug interaction
*aminoglycoside: DT, drug therapy
*aminoglycoside: PK, pharmacokinetics
*quinoline derived antiinfective agent: AE, adverse drug reaction
*quinoline derived antiinfective agent: DT, drug therapy
*macrolide: AE, adverse drug reaction
*macrolide: DT, drug therapy
*cephalosporin derivative: DO, drug dose
*cephalosporin derivative: IT, drug interaction
*cephalosporin derivative: DT, drug therapy
*cephalosporin derivative: PK, pharmacokinetics
*beta lactam antibiotic: DT, drug therapy
*benzathine penicillin: DT, drug therapy
procaine penicillin: DT, drug therapy
penicillin g sodium: DT, drug therapy
penicillin v potassium: CB, drug combination
penicillin v potassium: DT, drug therapy
penicillin g potassium: DT, drug therapy
penicillin g: DT, drug therapy
aminopenicillin: DT, drug therapy
amoxicillin: CB, drug combination
amoxicillin: DO, drug dose
amoxicillin: IT, drug interaction
amoxicillin: DT, drug therapy
amoxicillin: PK, pharmacokinetics
ampicillin: CB, drug combination
ampicillin: DO, drug dose
ampicillin: IT, drug interaction
ampicillin: DT, drug therapy
ampicillin: PK, pharmacokinetics
nafcillin: DT, drug therapy
oxacillin: DT, drug therapy
carbenicillin: DT, drug therapy

mezlocillin: DT, drug therapy
piperacillin: CB, drug combination
piperacillin: DT, drug therapy
ticarcillin: CB, drug combination
ticarcillin: DT, drug therapy
beta lactamase inhibitor: CB, drug combination
beta lactamase inhibitor: DT, drug therapy
clavulanic acid: CB, drug combination
clavulanic acid: DT, drug therapy
sulbactam: CB, drug combination
sulbactam: DT, drug therapy
tazobactam: CB, drug combination
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cefadroxil: DT, drug therapy
cefazolin: DT, drug therapy
cefalexin: DO, drug dose
cefalexin: DT, drug therapy
cefalotin: DT, drug therapy
cefradine: DT, drug therapy
cefaclor: DT, drug therapy
cefamandole: DT, drug therapy
cefonicid: DT, drug therapy
cefotetan: DT, drug therapy
cefoxitin: DO, drug dose
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cefprozil: DT, drug therapy
cefuroxime: DT, drug therapy
cefuroxime axetil: DT, drug therapy
cefepime: DT, drug therapy
cefixime: DT, drug therapy
cefoperazone: DT, drug therapy
cefotaxime: DT, drug therapy
cefpodoxime proxetil: DT, drug therapy
ceftazidime: DT, drug therapy
ceftibuten: DT, drug therapy
ceftizoxime: DT, drug therapy
ceftriaxone: DT, drug therapy
loracarbef: DT, drug therapy
cilastatin plus imipenem: CB, drug combination
cilastatin plus imipenem: DO, drug dose
cilastatin plus imipenem: IT, drug interaction
cilastatin plus imipenem: DT, drug therapy
cilastatin plus imipenem: PK, pharmacokinetics
meropenem: DT, drug therapy
aztreonam: DT, drug therapy
erythromycin: AE, adverse drug reaction
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azithromycin: DT, drug therapy
clarithromycin: AE, adverse drug reaction
clarithromycin: DT, drug therapy
dirithromycin: DT, drug therapy
levofloxacin: DT, drug therapy
lomefloxacin: DT, drug therapy
nalidixic acid: DT, drug therapy
norfloxacin: DT, drug therapy
ofloxacin: DT, drug therapy
sparfloxacin: DT, drug therapy
trovafloxacin: DT, drug therapy
amikacin: DT, drug therapy
gentamicin: DT, drug therapy
kanamycin: DT, drug therapy
neomycin: DT, drug therapy
netilmicin: DT, drug therapy

spectinomycin: DT, drug therapy
streptomycin: DT, drug therapy
tobramycin: DT, drug therapy
vancomycin: AE, adverse drug reaction
vancomycin: DT, drug therapy
ciprofloxacin
tobramycin sulfate
alatrofloxacin
enoxacin
meticillin
carindacillin
amoxicillin plus clavulanic acid
sultamicillin
orpeneed
beepen
penicillin v
bacampicillin
cloxacillin
dicloxacillin
cefapirin
cefamandole nafate
cefmetazole
piperacillin plus tazobactam
timentin

CAS REGISTRY NO.: (benzathine penicillin) 1538-09-6; (procaine penicillin) 54-35-3, 6130-64-9; (penicillin g sodium) 69-57-8; (penicillin v potassium) 132-98-9; (penicillin g potassium) 113-98-4, 1406-08-2; (penicillin g) 1406-05-9, 61-33-6; (amoxicillin) 26787-78-0, 61336-70-7; (ampicillin) 69-52-3, 69-53-4, 7177-48-2, 74083-13-9, 94586-58-0; (nafcillin) 147-52-4, 985-16-0; (oxacillin) 1173-88-2, 66-79-5, 7240-38-2; (carbenicillin) 17230-86-3, 4697-36-3, 4800-94-6; (mezlocillin) 42057-22-7, 51481-65-3; (piperacillin) 59703-84-3, 61477-96-1; (ticarcillin) 29457-07-6, 34787-01-4, 4697-14-7; (clavulanic acid) 58001-44-8; (sulbactam) 68373-14-8; (tazobactam) 93528-38-2; (cefadroxil) 50370-12-2; (cefazolin) 25953-19-9, 27164-46-1; (cefalexin) 15686-71-2, 23325-78-2; (cefalotin) 153-61-7, 58-71-9; (cefradine) 38821-53-3, 57584-26-6; (cefaclor) 53994-73-3; (cefamandole) 30034-03-8, 34444-01-4; (cefonicid) 61270-58-4, 61270-78-8; (cefotetan) 69712-56-7, 74356-00-6; (cefoxitin) 33564-30-6, 35607-66-0; (cefprozil) 92665-29-7; (cefuroxime) 55268-75-2, 56238-63-2; (cefuroxime axetil) 64544-07-6; (cefepime) 88040-23-7; (cefixime) 79350-37-1; (cefoperazone) 62893-19-0, 62893-20-3; (cefotaxime) 63527-52-6, 64485-93-4; (cefpodoxime proxetil) 87239-81-4; (ceftazidime) 72558-82-8; (ceftibuten) 97519-39-6; (ceftizoxime) 68401-81-0, 68401-82-1; (ceftriaxone) 73384-59-5, 74578-69-1; (loracarbef) 76470-66-1; (cilastatin plus imipenem) 92309-29-0; (meropenem) 96036-03-2; (aztreonam) 78110-38-0; (erythromycin) 114-07-8, 70536-18-4; (azithromycin) 83905-01-5; (clarithromycin) 81103-11-9; (dirithromycin) 62013-04-1; (levofloxacin) 100986-85-4, 138199-71-0; (lomefloxacin) 98079-51-7; (nalidixic acid) 389-08-2; (norfloxacin) 70458-96-7; (ofloxacin) 82419-36-1; (sparfloxacin) 111542-93-9; (trovafloxacin) 146836-84-2; (amikacin) 37517-28-5, 39831-55-5; (gentamicin) 1392-48-9, 1403-66-3, 1405-41-0; (kanamycin) 11025-66-4, 61230-38-4, 8063-07-8; (neomycin) 11004-65-2, 1404-04-2, 1405-10-3, 8026-22-0; (netilmicin) 56391-56-1, 56391-57-2; (spectinomycin) 1695-77-8, 21736-83-4, 23312-56-3; (streptomycin) 57-92-1; (tobramycin) 32986-56-4; (vancomycin) 1404-90-6, 1404-93-9;

(ciprofloxacin) 85721-33-1; (tobramycin sulfate) 49842-07-1; (alatrofloxacin) 157605-25-9; (enoxacin) 74011-58-8; (meticillin) 132-92-3, 38882-79-0, 61-32-5; (carindacillin) 26605-69-6, 35531-88-5; (amoxicillin plus clavulanic acid) 74469-00-4; (sultamicillin) 76497-13-7; (penicillin v) 87-08-1; (bacampicillin) 37661-08-8, 50972-17-3; (cloxacillin) 61-72-3, 642-78-4; (dicloxacillin) 13412-64-1, 3116-76-5, 343-55-5; (cefapirin) 21593-23-7, 24356-60-3; (cefamandole nafate) 42540-40-9; (cefmetazole) 56796-20-4, 56796-39-5; (timentin) 86482-18-0

CHEMICAL NAME: Trovan; Cipro; Pentrex; Levaquin; Maxaquin; Negram; Noroxin; Floxin; Zagam; Amikin; Garamycin; Kantrex; Mycifradin; Nebcin; Netromycin; Trobicin; Alatrofloxacin; Ciprofloxacin; Enoxacin; Staphcillin; Unipen; Nafcil; Prostaphlin; Geocillin; Mezlin; Pipracil; Ticar; Augmentin; Unasyn; Bicillin l a; Orpeneed; Pfizerpen; Beepen; **Pen vee**; Amoxil; Omnipen; Spectrobid; Cloxapen; Dycill; Duricef; Ancef; Keflex; Keflin; Cefadyl; Velosef; Ceclor; Mandol; Zefazone; Monocid; Cefotan; Mefoxin; Ceftin; Maxipime; Suprax; Cefobid; Claforan; Vantin; Fortaz; Cedax; Cefizox; Rocephin; Lorabid; Primaxin; Merrem; Azactam; Zithromax; Biaxin; Dynabac; Zosyn; Timentin; Nallpen; Pathocil; Tegopen; Wymox; Trimox; Ledercillin vk; Pentids; Wycillin

L14 ANSWER 4 OF 4 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91320774 EMBASE
DOCUMENT NUMBER: 1991320774
TITLE: The penicillins.
AUTHOR: Wright A.J.; Wilkowske C.J.
CORPORATE SOURCE: Mayo Clinic Proceedings, Siebens Building, Rochester, MN 55905, United States
SOURCE: Mayo Clinic Proceedings, (1991) 66/10 (1047-1063). ISSN: 0025-6196 CODEN: MACPAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:

The penicillin family of antibiotics remains an important part of our antimicrobial armamentarium. In general, these agents have bactericidal activity, excellent distribution throughout the body, low toxicity, and efficacy against infections caused by susceptible bacteria. The initial introduction of aqueous penicillin G for treatment of streptococcal and staphylococcal infections was an important pharmacologic landmark. The emergence of penicillinase-producing Staphylococcus aureus prompted the development of the penicillinase-resistant penicillins (for example, methicillin, oxacillin, and nafcillin), in which an acyl side chain prevented disruption of the .beta.-lactamase ring. Subsequently, the aminopenicillins (such as ampicillin and amoxicillin) were developed because of the need for gram-negative antimicrobial activity. Their spectrum included Escherichia coli, Proteus mirabilis, Shigella, Salmonella, Listeria, Haemophilus, and Neisseria. The search for a penicillin with additional antimicrobial activity against the Enterobacteriaceae and Pseudomonas aeruginosa led to the development of the carboxypenicillins (carbenicillin, ticarcillin, and temocillin) and the ureidopenicillins (mezlocillin, azlocillin, piperacillin, and apalcillin). Finally, the combination of a .beta.-lactamase **inhibitor** (clavulanic acid or sulbactam) and an aminopenicillin or ticarcillin has further extended their antibacterial spectra. The development of an ideal penicillin that is rapidly bactericidal, nonsensitizing, nontoxic, bioavailable, resistant to

.beta.-lactamase, and without inoculum effect and that has a high affinity for penicillin-binding proteins remains the goal.

CONTROLLED TERM: Medical Descriptors:
*antimicrobial therapy
conference paper
priority journal
Drug Descriptors:
*penicillin derivative
amoxicillin
amoxicillin plus clavulanic acid
ampicillin
apalcillin
azlocillin
bacampicillin
bactocill
benzathine penicillin
carbenicillin
clavulanic acid
cloxacillin
cyclacillin
dicloxacillin
foramdinocillin
hetacillin
mecillinam
meticillin
mezlocillin
nafcillin
oxacillin
pathocill
penapar
penicillin g
penicillin g potassium
penicillin v
pheneticillin
piperacillin
pivmecillinam
procaine penicillin
sulbactam
sultamicillin
temocillin
ticarcillin
timentin
unclassified drug

CAS REGISTRY NO.: (amoxicillin) 26787-78-0, 61336-70-7; (amoxicillin plus clavulanic acid) 74469-00-4; (ampicillin) 69-52-3, 69-53-4, 7177-48-2, 74083-13-9, 94586-58-0; (apalcillin) 58795-03-2, 63469-19-2; (azlocillin) 37091-65-9, 37091-66-0; (bacampicillin) 37661-08-8, 50972-17-3; (benzathine penicillin) 1538-09-6; (carbenicillin) 17230-86-3, 4697-36-3, 4800-94-6; (clavulanic acid) 58001-44-8; (cloxacillin) 61-72-3, 642-78-4; (cyclacillin) 3485-14-1; (dicloxacillin) 13412-64-1, 3116-76-5, 343-55-5; (hetacillin) 3511-16-8, 5321-32-4; (mecillinam) 32887-01-7; (meticillin) 132-92-3, 38882-79-0, 61-32-5; (mezlocillin) 42057-22-7, 51481-65-3; (nafcillin) 147-52-4, 985-16-0; (oxacillin) 1173-88-2, 66-79-5, 7240-38-2; (penicillin g) 1406-05-9, 61-33-6; (penicillin g potassium) 113-98-4, 1406-08-2; (penicillin v) 87-08-1; (pheneticillin) 132-93-4, 147-55-7; (piperacillin) 59703-84-3, 61477-96-1; (pivmecillinam) 32886-97-8, 32887-03-9; (procaine penicillin) 54-35-3, 6130-64-9; (sulbactam) 68373-14-8; (sultamicillin) 76497-13-7; (temocillin) 61545-06-0, 66148-78-5; (ticarcillin) 29457-07-6, 34787-01-4,

4697-14-7; (timentin) 86482-18-0
CHEMICAL NAME: Pentids; Pfizerpen; Wycillin; Duracillin; Bicillin; Permapen; **Pen vee**; V cillin; Broxil; Syncillin; Maxipen; Staphcillin; Prostaphlin; Unipen; Nafcil; Nallpen; Tegopen; Cloxapen; Dynapen; Dycill; Polycillin; Omnipen; Amoxil; Polymox; Spectrobid; Versapen; Cyclapen; Geopen; Ticar; Mezlin; Pipracil; Coactin; Augmentin; Timentin; Unasyn; Penapar; Bactocill; Pathocill; Wymox

=> d his

(FILE 'HOME' ENTERED AT 12:51:36 ON 12 MAY 2003)

FILE 'MEDLINE, BIOSIS, BIOTECHDS, CAPLUS, EMBASE' ENTERED AT 12:51:44 ON 12 MAY 2003
L1 2090 S (VENEZUELAN EQUINE ENCEPHALITIS VIRUS) OR VEE
L2 168238 S CELL (A) DEATH
L3 9 S L1 AND L2

FILE 'STNGUIDE' ENTERED AT 12:55:12 ON 12 MAY 2003
L4 32 S INHIBITOR OR DRUG

FILE 'MEDLINE, BIOSIS, BIOTECHDS, CAPLUS, EMBASE' ENTERED AT 12:58:58 ON 12 MAY 2003
L5 1312299 S INHIBITOR OR DRUG AND APOPTOSIS
L6 0 S L3 AND L5
L7 0 S L3 AND INHIBITOR
L8 101757 S (INHIBITOR OR DRUG) AND APOPTOSIS
L9 103106 S DRUG SCREENING
L10 2198 S L8 AND L9
L11 1493 S VEE
L12 0 S L10 AND L11
L13 1256865 S INHIBITOR
L14 4 S L11 AND L13

=> s l1 and l13
L15 10 L1 AND L13

=> dup rem l15
PROCESSING COMPLETED FOR L15
L16 10 DUP REM L15 (0 DUPLICATES REMOVED)

=> d iall l16 1-10

L16 ANSWER 1 OF 10 BIOTECHDS COPYRIGHT 2003 THOMSON DERWENT AND ISI
ACCESSION NUMBER: 2002-09805 BIOTECHDS
TITLE: Composition useful for treating or preventing HIV infections, comprises two or more isolated nucleic acids encoding env, gag or pol gene product of HIV or immunogenic fragment of the gene products;
vaccine composition having virus-like particle inhibition, integrase-**inhibitor**, RNA-ase-H-**inhibitor** and reverse-transcriptase-**inhibitor** activity, useful for virus infection gene therapy
AUTHOR: OLMSTED R; KEITH P; DRYGA S; CALEY I; MAUGHAN M; JOHNSTON R; DAVIS N; SWANSTROM R
PATENT ASSIGNEE: ALPHAVAX INC; UNIV NORTH CAROLINA
PATENT INFO: WO 2002003917 17 Jan 2002
APPLICATION INFO: WO 2000-US21701 7 Jul 2000
PRIORITY INFO: US 2000-216995 7 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-171664 [22]

ABSTRACT:

DERWENT ABSTRACT:
NOVELTY - A composition (I) comprising isolated nucleic acids (II) encoding env, gag or pol gene product of human immunodeficiency virus or immunogenic fragment of the gene products, is new. The gag gene product is modified to inhibit formation of virus-like particles containing gag gene product and their release from cells, and the pol gene product is modified to inhibit reverse transcriptase activity.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a composition (III) comprising a population of alpha-virus replicon particles (IV) or a population of alpha-virus replicon virosomes (V) comprising (II), where the nucleic acids are each contained within a separate alpha-virus replicon particle or virosome; (2) making (M1) (IV) by: (a) providing a first, second or third helper cell for producing a first, second or third population of infectious replication defective alpha-virus particles, comprising in a alpha-virus-permissive cell: (i) an alpha-virus replicon RNA, wherein the replicon RNA comprises an alpha-virus packaging signal (II) and the replicon RNA lacks sequence encoding alpha-virus structural proteins; (ii) a first helper RNA separate from the replicon RNA, where the first helper RNA encodes at least one alpha-virus structural protein and does not encode at least one other alpha-virus structural protein; and (iii) one or more additional helper RNAs separate from the replicon RNA and separate from the first helper RNA, where the additional helper RNAs encodes at least one other alpha-virus structural protein not encoded by the first helper RNA, and where at least one of the helper RNA is lacking an alpha-virus packaging signal, where the combined expression of the alpha-virus replicon RNA and the helper RNAs produces an assembled alpha-virus particle which is able to infect a cell and is unable to complete viral replication, and the first, second or third population contains no detectable replication-competent alpha-virus particles as determined by passage on permissive cells in culture; (b) producing the alpha-virus particles in the helper cell, and collecting the alpha-virus particles from the helper cells; and (c) combining the first, second and third population of alpha-virus particles produced from the first, second and third helper cells, respectively, thus producing (IV); (3) a population of alpha-virus replicon particles produced by M1; (4) producing (M2) (V), by producing a first, second and third population of alpha-virus replicon virosomes by combining alpha-virus replicon RNA comprising (II), alpha-virus glycoproteins E1 and E2, non-cationic lipids and detergent, gradually removing detergent, where alpha-virus replicon virosomes are produced, and combining the first, second and third population of alpha-virus replicon virosomes to produce (V); (5) an alpha-virus replicon virosome (VI) comprising an alpha-virus replicon RNA encapsulated by a lipid bilayer comprising alpha-virus glycoproteins, E1 and E2; (6) producing (M3) (VI); (7) an alpha-virus replicon virosome produced by M3; (8) a composition (VII) comprising heparin affinity-purified alpha-virus replicon particles (VIII) which comprises at least one structural protein comprising one or more attenuating mutations; (9) preparing (M4) (VIII); (10) a composition produced by M4; (11) producing (M5) an alpha-virus replicon particle (VRP) for use in vaccine; (12) VRP (IX) produced by M5; (13) an isolated nucleic acid (X) encoding a pol gene product of HIV or its immunogenic fragment, where the pol gene produce comprises the modification resulting in deletion or inactivation of

integrase, RNase H and reverse transcriptase functions in the pol gene product; (14) a composition (XI) comprising (X); (15) a vector (XII) comprising (X); (16) a cell (XIII) comprising (XII); (17) an alpha-virus replicon particle (XIV) comprising (X); (18) production (M6) of (XIV), comprising culturing (XIII); and (19) an alpha-virus replicon particle produced by M6.

BIOTECHNOLOGY - Preferred Composition: In (III), the alpha-virus replicon particles comprise a replicon RNA or at least one structural protein which comprises one or more attenuating mutations. The pol gene product comprises a modification resulting in deletion or inactivation of integrase, RNase H and reverse transcriptional functions in the pol gene product. Preferred Method: In M1, the replicon RNA, the first helper RNA, and one or more additional helper RNAs comprises one or more attenuating mutations. The alpha-virus replicon RNA of at least one of the first, second and third helper cell comprises a sequence encoding at least one alpha-virus structural coating, where the first helper RNA and one or more additional helper RNAs in the first, second, and third helper cell, encodes at least one other alpha-virus structural coatings not encoded by the replicon RNA. Preferred Virosome: In (VI), the alpha-virus glycoproteins are Venezuelan Equine Encephalitis glycoproteins E1 and E2.

ACTIVITY - Anti-HIV (human immunodeficiency virus).

MECHANISM OF ACTION - Vaccine; inducer of immune response (claimed). Immunological response of mice to alpha-virus replicon particles (VRP)-gag vaccine was tested: Mice were injected subcutaneously in two doses, with 8-9 mice in each group. The mice were immunized once, then immunized a second time, with the same dose, 28 days later. Serum was collected the day prior to the first immunization, then at day 27 (after 1st immunization) and at day 35 (after 2nd immunization). The mice showed a vigorous, antigen-specific humoral response to HIV-1 Clade C VRP-gag vaccine.

USE - (I), (III), (IV), (VI) or (XI) is useful for inducing an immune response to human immunodeficiency virus (HIV) or for treating or preventing HIV infection in a subject. (IX) is useful in a vaccine. (All claimed). (I) or (III) is useful for administering a protein or peptide to a subject. (VII) is useful as a clinical trial material and commercial product.

ADMINISTRATION - (III) is administered by parenteral (e.g. subcutaneous, intradermal, intramuscular, intravenous, intraarticular) or intranasal route at a dose of 10 to the power 3-10 to the power 7, preferably 10 to the power 4-10 to the power 6 alpha-virus replicon particles.

ADVANTAGE - (VI) is easy to prepare, stable, and pure, since it is devoid of any cellular components being made in a cell free system.

EXAMPLE - Replicon particles for use as a vaccine were produced using the **Venezuelan Equine Encephalitis virus** (**VEE**)-based vector system, originally developed from a full-length, infectious cDNA clone of the RNA genome of **VEE**. One or more attenuating mutations were inserted into the clone to generate attenuated **VEE** vaccine vectors. The constructs were genetically modified to create an RNA replicon, and one or more helper RNAs to allow packaging. The replicon RNA expressed an HIV gene, e.g. the Clade C HIV-1 gag gene. The replicon RNA was packaged into virus-like particles (virus replicon particles or VRPs) that were infectious for only one cycle. During this cycle, the

characteristics of the alpha-virus-based vector resulted in very high levels of expression of the replicon RNA in cells to which the VRP was targeted. In the cytoplasm of the target cell, the replicon RNA was first translated to produce viral replicase proteins necessary to initiate self-amplification and expression. The HIV-1 Clade C gag gene was encoded by a subgenomic mRNA, abundantly transcribed from a negative-sense replicon RNA intermediate, leading to high-level expression of HIV-1 Clade C gag product. Since the **VEE** structural protein genes were not encoded by the replicon RNA, progeny virion particles were not assembled, thus limiting to a single cycle within the infected target cell. Only the replicon RNA was packaged into VRPs, as the helper RNAs lacked the cis-acting packaging sequence required for encapsidation. The split helper or bipartite system greatly reduced the chance for an intact genome being assembled by recombination, and as a back-up safety feature, one or more highly attenuating mutations, such as those contained in the glycoprotein genes in V3014 were incorporated. Overall, the design of the VRPs incorporated several layered and redundant safety features. In addition to the above-described split helper system and attenuating mutations, over one-third of the genome of the virus was removed, creating a defective genome which prevented spread from the initially infected target cell. If a statistically rare recombination event occurred to yield replication competent virus (RCV), the resulting virus was a highly attenuated **VEE** strain.(201 pages)

CLASSIFICATION: PHARMACEUTICALS, Vaccines; GENETIC TECHNIQUES and APPLICATIONS, Gene Expression Techniques and Analysis; DISEASE, HIV and Other Virus Infections; THERAPEUTICS, Gene Therapy

CONTROLLED TERMS: COMPOSITION CHARACTERIZATION, HIV VIRUS MUTANT ENV, GAG, POL GENE, VENEZUELAN-HORSE-ENCEPHALITIS VIRUS VECTOR, HOST CELL INFECTION, ALPHA VIRUS GLYCOPROTEIN, VIRUS-LIKE PARTICLE INHIBITION, INTEGRASE-**INHIBITOR**,RNA-ASE-H-**INHIBITOR**, REVERSE-TRANSCRIPTASE-**INHIBITOR** ACT., APPL. VIRUS INFECTION THERAPY, GENE THERAPY, NUCLEIC ACID VACCINE, RECOMBINANT VACCINE, CLINICAL TRIAL LEUKO VIRUS RETRO VIRUS AIDS LENTI VIRUS ARBO VIRUS ENZYME-**INHIBITOR** IMMUNOSTIMULANT (21, 32)

L16 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:435247 CAPLUS

DOCUMENT NUMBER: 135:41796

TITLE: Replicon-based activation of endogenous genes using genetic elements for RNA replication

INVENTOR(S): Hennecke, Frank; Renner, Wolfgang A.

PATENT ASSIGNEE(S): Cytos Biotechnology A.-G., Switz.

SOURCE: PCT Int. Appl., 131 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:
MAIN: C12N015-00

CLASSIFICATION: 3-2 (Biochemical Genetics)

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042442	A2	20010614	WO 2000-IB1841	20001208
WO 2001042442	A3	20011122		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002168709 A1 20021114 US 2000-733042 20001211
PRIORITY APPLN. INFO.: US 1999-169988P P 19991210

ABSTRACT:
The present invention relates to methods for the modification of genomes of eukaryotic cells to alter the expression of endogenous genes. The invention further relates to vector systems useful for modifying the genomes of eukaryotic cells to alter the expression of endogenous genes. Homologous recombination is performed using a two-component vector system, comprising a 5' targeting construct and a 3'- targeting construct. The 5' targeting construct contains the following subcomponents: (a) a 5' targeting sequence; (b) a 5' cis-acting replication element which, in conjunction with a 3' cis-acting replication element, allows for multiple rounds of RNA amplification; (c) nucleic acid encoding alphaviral nonstructural protein 1-4 (nsP1-4); (d) a resistance marker cassette, consisting of a resistance marker operably linked to a first alphaviral subgenomic promoter, both of which are located between two loxP recombination sites; (e) a second subgenomic promoter; and (f) a 3' targeting sequence. The 3' targeting construct contains the following subcomponents: (a) a 5' targeting sequence; (b) a 3' cis-acting replication element; (c) nucleic acid encoding a poly(A) stretch; (d) nucleic acid encoding a hepatitis delta virus antigenomic ribozyme; (e) a transcription terminator and polyadenylation signal; (f) a resistance marker operably linked to an RNA polymerase II promoter; and (g) a 3' targeting sequence. A strategy is presented for activation of the chromosomal erythropoietin gene using the alphavirus replicon-based approach.

SUPPL. TERM: RNA replication replicon gene activation targeting

INDEX TERM: Animal cell line
(HEP-3B; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Animal cell line
(Hep G2; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Metallothioneins
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(I, selection marker; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Metallothioneins
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(II, selection marker; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Genetic element
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(IRES (internal ribosomal entry site) element; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Lipoprotein receptors
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(LDL; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Recombination, genetic

(amplification; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Genetic element
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(cis-acting replication element; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Toxins
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(diphtheria, selection marker; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Ribozymes
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(hepatitis delta; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Recombination, genetic
(homologous; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Animal cell
(mammalian; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Proteins, specific or class
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(nonstructural, nsP1-4; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Genetic markers
(pos. and neg. selection; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Gene
(regulation; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: RNA formation
(replication; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Alphavirus
Animal cell
Gene targeting
Kidney
Liver
Organ, animal
Replicon
Ross River virus
Semliki Forest virus
Sindbis virus
Testis
Venezuelan equine encephalitis virus
(replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Interleukin 2
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Promoter (genetic element)
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(subgenomic; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Interferons
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(.alpha.; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Interferons
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(.beta.; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: Interferons
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(.gamma.; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: 9000-94-6P, Antithrombin III 9001-25-6P, Blood-coagulation factor VII 9001-27-8P, Blood-coagulation factor VIII 9001-28-9P, Blood-coagulation factor IX 9002-72-6P, Growth hormone 9004-10-8P, Insulin, preparation 9014-42-0P, Megakaryocyte growth and development factor 9025-35-8P, .alpha.-Galactosidase 9041-92-3P, .alpha.1-Trypsin **inhibitor** 11096-26-7P, Erythropoietin 83869-56-1P, GM-CSF 139639-23-9P, Tissue plasminogen activator
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: 9002-03-3, Dihydrofolate reductase 9002-06-6, Thymidine kinase 9014-52-2, Tryptophan synthase 9016-12-0, Hypoxanthine phosphoribosyltransferase 9025-05-2, Cytosine deaminase 9028-27-7, Histidinol dehydrogenase 37350-22-4, Xanthine-guanine phosphoribosyltransferase 62213-36-9, Neomycin phosphotransferase 88361-67-5, Hygromycin B phosphotransferase
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(selection marker; replicon-based activation of endogenous genes using genetic elements for RNA replication)

INDEX TERM: 337830-95-2, 1: PN: WO0142442 SEQID: 1 unclaimed DNA 344805-65-8 344805-66-9 344805-67-0 344805-68-1 344805-69-2 344805-70-5, 7: PN: WO0142442 SEQID: 7 unclaimed DNA 344805-71-6 344805-72-7 344805-73-8 344805-74-9 344805-75-0 344805-76-1 344805-77-2 344805-78-3 344805-79-4 344805-80-7 344805-81-8 344805-82-9 344805-83-0 344805-84-1 344805-85-2 344805-86-3 344805-87-4 344805-88-5 344805-89-6 344805-90-9 344805-91-0 344805-92-1 344805-93-2 344805-94-3 344805-95-4 344805-96-5 344805-97-6 344805-98-7 344805-99-8 344806-00-4 344806-01-5 344806-02-6 344806-03-7 344806-04-8 344806-05-9 344806-06-0 344806-07-1 344806-08-2 344806-09-3 344820-79-7 344820-80-0 344820-83-3
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; replicon-based activation of endogenous genes using genetic elements for RNA replication)

L16 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:530500 CAPLUS
DOCUMENT NUMBER: 136:256743

TITLE: Combined therapy of experimental tumors with the vaccinal strain of Venezuelan encephalomyelitis virus

AUTHOR(S): Urazova, L. N.; Gromova, A. Yu.
CORPORATE SOURCE: NII Onkol., Tomsk. Nauchnyi Tsentr, SO RAMN, Tomsk, Russia

SOURCE: Voprosy Onkologii (2001), 47(1), 78-80
CODEN: VOONAW; ISSN: 0507-3758
PUBLISHER: Eskulap
DOCUMENT TYPE: Journal
LANGUAGE: Russian
CLASSIFICATION: 1-4 (Pharmacology)
Section cross-reference(s): 10

ABSTRACT:
The potential of therapy with vaccinal strain of Venezuelan encephalomyelitis virus (VEL) in conjunction with cytostatic (cyclophosphamide) or immunomodulator (T-activin) has been studied. It was found that VEL in conjunction with cyclophosphamide inhibited the antitumor action of the drugs while T-activin potentiated the same effects of the virus and its oncolyzate.

SUPPL. TERM: cyclophosphamide interaction Venezuelan encephalomyelitis virus strain antitumor; Tactivin immunomodulator potentiation VEL vaccinal strain anticancer; lung antimetastatic melanoma **inhibitor** cytostatic VEL strain interaction; adenocarcinoma **inhibitor** immunomodulator VEL strain additive interaction

INDEX TERM: Drug interactions
(additive; combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

INDEX TERM: Antitumor agents
(adenocarcinoma; combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

INDEX TERM: Cytotoxic agents
Drug interactions
Immunomodulators
(combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

INDEX TERM: Antitumor agents
(lung, metastasis; combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

INDEX TERM: Antitumor agents
(melanoma, metastasis; combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

INDEX TERM: Lung, neoplasm
(metastasis, inhibitors; combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

INDEX TERM: Drug interactions
(potentiation; combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

INDEX TERM: **Venezuelan equine encephalitis virus**
(vaccinal strain of; combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

INDEX TERM: 50-18-0, Cyclophosphamide 89492-35-3, T-Activin
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combined therapy of exptl. tumors with the vaccinal strain of Venezuelan encephalomyelitis virus)

ACCESSION NUMBER: 2001:570167 BIOSIS
DOCUMENT NUMBER: PREV200100570167
TITLE: Early onset of virus infection in brain by Tunicamycin: Possible role of cytokines.
AUTHOR(S): Seth, P. (1); Steele, K. (1); Husain, M. M.; Gupta, P.; Catlin, K. (1); Schoneboom, B. A. (1); Grieder, F. (1); Maheshwari, R. K. (1)
CORPORATE SOURCE: (1) Uniformed Services University of the Health Sciences, Bethesda, MD, 20814 USA
SOURCE: Journal of Interferon and Cytokine Research, (2001) Vol. 24, No. Supplement 1, pp. S.136-S.137. print.
Meeting Info.: Annual Meeting of the International Society for Interferon and Cytokine Research Cleveland,, OH, USA October 07-11, 2001
ISSN: 1079-9907.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals *00520
Biochemical Studies - General *10060
Nervous System - Physiology and Biochemistry *20504
Virology - Animal Host Viruses *33506
Medical and Clinical Microbiology - Virology *36006
BIOSYSTEMATIC CODE: Togaviridae 02626
Muridae 86375
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Infection; Nervous System (Neural Coordination)
INDEX TERMS: Parts, Structures, & Systems of Organisms
CNS [central nervous system]: nervous system; brain: nervous system
INDEX TERMS: Diseases
Venezuelan equine encephalitis virus infection: viral disease
INDEX TERMS: Chemicals & Biochemicals
tunicamycin: glycoside **inhibitor**
INDEX TERMS: Miscellaneous Descriptors
neurodegeneration; Meeting Abstract; Meeting Poster
ORGANISM: Super Taxa
Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Togaviridae: Animal Viruses, Viruses, Microorganisms
ORGANISM: Organism Name
Semliki Forest Virus (Togaviridae): pathogen; **Venezuelan equine encephalitis virus** (Togaviridae): pathogen; mouse (Muridae): animal model
ORGANISM: Organism Superterms
Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; Viruses
REGISTRY NUMBER: 11089-65-9 (TUNICAMYCIN)

L16 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:470323 CAPLUS
DOCUMENT NUMBER: 133:100441
TITLE: Method for molecular cloning genes encoding proteins with predetermined property by using viral expression vectors
INVENTOR(S): Bailey, James E.; Renner, Wolfgang A.; Orberger, Georg H.; Koller, Daniel
PATENT ASSIGNEE(S): Cytos Biotechnology G.M.B.H, Switz.
SOURCE: Jpn. Kokai Tokkyo Koho, 192 pp.

CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
INT. PATENT CLASSIF.: C12N015-09; C07K014-01; C07K014-705; C12N001-15; C12N001-19; C12N005-10; C12N007-00; C12P021-02; C12Q001-68; G01N033-566; G01N033-50
CLASSIFICATION: 3-2 (Biochemical Genetics)
Section cross-reference(s): 1, 6
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000189173	A2	20000711	JP 1999-236220	19990823
WO 9925876	A1	19990527	WO 1998-US24520	19981117
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6524792	B1	20030225	US 1998-193707	19981117

PRIORITY APPLN. INFO.:
US 1998-193707 A 19981117
WO 1998-US24520 W 19981117
US 1997-972218 A2 19971117

ABSTRACT:
The present invention provides methods for rapid identifying, characterizing and isolating proteins with predetd. properties such as cellular localization, structure, affinity to a binding partner and enzymic activities. The invention also provides expression systems which could selectively express the exogenous proteins while the expression of endogenous proteins in a host is suppressed. Also disclosed are the uses of viral expression vectors such as the alpha virus, which have the ability to block host protein synthesis by expressing viral genome. The invention also relates to constructing a expression vector contg. promoters or enhancers specific for RNA polymerase I or III to render the expression of exogenous proteins dependent upon RNA polymerase I or III, therefore, the transcription of host cellular genes could be arrested by adding an RNA polymerase II specific inhibiter while the expression of exogenous genes carried by the expression vector would not be affected. In an embodiment of the invention, a defective helper RNA is used to facilitate the propagation of the virus with large insert of exogenous DNAs. In another embodiment of the invention, the exogenous protein encoded by the expression system could be distinguished from the endogenous proteins of the host cell system by specific labeling during a time window in which endogenous protein expression is suppressed while the exogenous protein is expressed. The invention is further relates to the uses of methods and expression systems of this invention in diagnosis, therapy and drug screening.

SUPPL. TERM: protein expression system viral vector mol cloning
INDEX TERM: Proteins, specific or class
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(PE2; E2; E3; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)
INDEX TERM: Eukaryote (Eukaryotae)
(as host cells; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)
INDEX TERM: Body space
(extracellular; method for mol. cloning genes encoding proteins with predetd. property by using viral expression

vectors)

INDEX TERM: Proteins, specific or class
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(labeled; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Proteins, specific or class
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(ligand-binding; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Receptors
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(membrane assocd.; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Proteins, specific or class
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(membrane, receptor; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Alphavirus
Genetic vectors
Molecular cloning
Semliki Forest virus
Transcriptional regulation
Venezuelan equine encephalitis virus
Virus vectors
(method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Transgene
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Enzymes, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(protein has activities of; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Cell membrane
Cell nucleus
Cytoplasm
Endoplasmic reticulum
Endosome
Golgi apparatus
Lysosome
Mitochondria
Peroxisome
(protein localized on; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Genetic element
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(regulatory, specific for RNA polymerase I or III; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Proteins, specific or class

ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(secretory; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Culture media
(semi-solid; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Sindbis virus
(temp. sensitive strains: ts20; ts10; and ts23; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Gene, microbial
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(vir; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Chromatography
Filtration
Precipitation (chemical)
(viral particles are sepd. from exogenous protein by; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: Proteins, specific or class
ROLE: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(with predetd. property; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: 9014-24-8
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(II; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: 50-76-0, Actinomycin D 1162-65-8, Aflatoxin b1
11030-71-0, Amatoxin 37205-61-1, Protease **inhibitor**
ROLE: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: 273948-51-9, 5: PN: WO0032227 SEQID: 4 unclaimed DNA
282120-87-0 282120-88-1 282120-89-2 282120-90-5
282120-91-6 282120-92-7 282120-93-8 282120-94-9
282120-95-0
ROLE: PRP (Properties)
(unclaimed nucleotide sequence; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

INDEX TERM: 282737-36-4 282737-37-5 282737-38-6 282737-39-7
282737-40-0 282737-41-1 282737-42-2 282737-43-3
282737-44-4 282737-45-5 282737-46-6 282737-47-7
282737-48-8 282737-49-9 282737-50-2 282737-51-3
282737-52-4 282737-53-5 282737-54-6 282737-55-7
282737-56-8 282737-57-9
ROLE: PRP (Properties)
(unclaimed sequence; method for mol. cloning genes encoding proteins with predetd. property by using viral expression vectors)

L16 ANSWER 6 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:52043 BIOSIS
DOCUMENT NUMBER: PREV200000052043

TITLE: Perspective: Virus infections and the death of neurons.
AUTHOR(S): Griffin, Diane E. (1); Hardwick, J. Marie (1)
CORPORATE SOURCE: (1) Dept of Molecular Microbiology and Immunology, Johns Hopkins University School of Hygiene and Public Health, 615 N. Wolfe St, Baltimore, MD USA
SOURCE: Trends in Microbiology, (April, 1999) Vol. 7, No. 4, pp. 155-160.
ISSN: 0966-842X.
DOCUMENT TYPE: General Review
LANGUAGE: English
CONCEPT CODE: Medical and Clinical Microbiology - Virology *36006
Cytology and Cytochemistry - Animal *02506
Biochemical Studies - General *10060
Nervous System - Pathology *20506
BIOSYSTEMATIC CODE: Bunyaviridae - animal host only 02605
Flaviviridae 02609
Reoviridae - animal host only 02622
Togaviridae 02626
Muridae 86375
INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Infection; Nervous System (Neural Coordination)
INDEX TERMS: Diseases
viral encephalitis: nervous system disease, viral disease
INDEX TERMS: Chemicals & Biochemicals
Bcl protein family; CrmA: protease **inhibitor**; caspase; nerve growth factor; tumor necrosis factor receptor
INDEX TERMS: Alternate Indexing
Encephalitis, Viral (MeSH)
INDEX TERMS: Methods & Equipment
terminal transferase technique [TUNEL technique]: analytical method
INDEX TERMS: Miscellaneous Descriptors
cytoplasmic blebbing; neuronal apoptosis
ORGANISM: Super Taxa
Bunyaviridae (animal host only): Animal Viruses, Viruses, Microorganisms; Flaviviridae: Animal Viruses, Viruses, Microorganisms; Muridae: Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Reoviridae (animal host only): Animal Viruses, Viruses, Microorganisms; Togaviridae: Animal Viruses, Viruses, Microorganisms
ORGANISM: Organism Name
LaCrosse virus (Bunyaviridae (animal host only)); Semliki Forest virus (Togaviridae); Sindbis virus (Togaviridae); **Venezuelan equine encephalitis virus** (Togaviridae); dengue virus (Flaviviridae); mouse (Muridae): animal model, host; reovirus (Reoviridae (animal host only))
ORGANISM: Organism Superterms
Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; Viruses
REGISTRY NUMBER: 186322-81-6 (CASPASE)
9061-61-4 (NERVE GROWTH FACTOR)

L16 ANSWER 7 OF 10 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999106908 EMBASE
TITLE: Systemic antibiotics: A review and their use in chronic wounds.
AUTHOR: Hernandez R. Jr.
CORPORATE SOURCE: Dr. R. Hernandez Jr., Department of Medicine, Univ. of Miami School of Medicine, Miami, FL, United States
SOURCE: Dermatologic Therapy, (1999) 9/- (44-62).

Refs: 72
ISSN: 1396-0296 CODEN: DETHFE
COUNTRY: Denmark
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
013 Dermatology and Venereology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

CONTROLLED TERM: Medical Descriptors:
*wound care
*wound healing
*antimicrobial activity
*wound infection: DR, drug resistance
*wound infection: DT, drug therapy
drug use
antibiotic resistance
drug structure
nausea: SI, side effect
diarrhea: SI, side effect
vomiting: SI, side effect
abdominal pain: SI, side effect
heart ventricle tachycardia: SI, side effect
heart arrest: SI, side effect
drug contraindication
arthropathy: SI, side effect
ototoxicity: SI, side effect
nephrotoxicity: SI, side effect
disease association
insulin dependent diabetes mellitus
immunocompetence
neutropenia
human immunodeficiency virus infection
kidney failure
aging
human
oral drug administration
intramuscular drug administration
intravenous drug administration
topical drug administration
review
Drug Descriptors:
*aminoglycoside: AE, adverse drug reaction
*aminoglycoside: DO, drug dose
*aminoglycoside: IT, drug interaction
*aminoglycoside: DT, drug therapy
*aminoglycoside: PK, pharmacokinetics
*quinoline derived antiinfective agent: AE, adverse drug reaction
*quinoline derived antiinfective agent: DT, drug therapy
*macrolide: AE, adverse drug reaction
*macrolide: DT, drug therapy
*cephalosporin derivative: DO, drug dose
*cephalosporin derivative: IT, drug interaction
*cephalosporin derivative: DT, drug therapy
*cephalosporin derivative: PK, pharmacokinetics
*beta lactam antibiotic: DT, drug therapy
*benzathine penicillin: DT, drug therapy
procaine penicillin: DT, drug therapy
penicillin g sodium: DT, drug therapy
penicillin v potassium: CB, drug combination
penicillin v potassium: DT, drug therapy

penicillin g potassium: DT, drug therapy
penicillin g: DT, drug therapy
aminopenicillin: DT, drug therapy
amoxicillin: CB, drug combination
amoxicillin: DO, drug dose
amoxicillin: IT, drug interaction
amoxicillin: DT, drug therapy
amoxicillin: PK, pharmacokinetics
ampicillin: CB, drug combination
ampicillin: DO, drug dose
ampicillin: IT, drug interaction
ampicillin: DT, drug therapy
ampicillin: PK, pharmacokinetics
nafcillin: DT, drug therapy
oxacillin: DT, drug therapy
carbenicillin: DT, drug therapy
mezlocillin: DT, drug therapy
piperacillin: CB, drug combination
piperacillin: DT, drug therapy
ticarcillin: CB, drug combination
ticarcillin: DT, drug therapy
beta lactamase inhibitor: CB, drug combination
beta lactamase inhibitor: DT, drug therapy
clavulanic acid: CB, drug combination
clavulanic acid: DT, drug therapy
sulbactam: CB, drug combination
sulbactam: DT, drug therapy
tazobactam: CB, drug combination
tazobactam: DT, drug therapy
cefadroxil: DT, drug therapy
cefazolin: DT, drug therapy
cefalexin: DO, drug dose
cefalexin: DT, drug therapy
cefalotin: DT, drug therapy
cefradine: DT, drug therapy
cefaclor: DT, drug therapy
cefamandole: DT, drug therapy
cefonicid: DT, drug therapy
cefotetan: DT, drug therapy
cefoxitin: DO, drug dose
cefoxitin: DT, drug therapy
cefprozil: DT, drug therapy
cefuroxime: DT, drug therapy
cefuroxime axetil: DT, drug therapy
cefepime: DT, drug therapy
cefixime: DT, drug therapy
cefoperazone: DT, drug therapy
cefotaxime: DT, drug therapy
cefpodoxime proxetil: DT, drug therapy
ceftazidime: DT, drug therapy
ceftibuten: DT, drug therapy
ceftizoxime: DT, drug therapy
ceftriaxone: DT, drug therapy
loracarbef: DT, drug therapy
cilastatin plus imipenem: CB, drug combination
cilastatin plus imipenem: DO, drug dose
cilastatin plus imipenem: IT, drug interaction
cilastatin plus imipenem: DT, drug therapy
cilastatin plus imipenem: PK, pharmacokinetics
meropenem: DT, drug therapy
aztreonam: DT, drug therapy
erythromycin: AE, adverse drug reaction
erythromycin: DT, drug therapy
azithromycin: AE, adverse drug reaction

azithromycin: DT, drug therapy
clarithromycin: AE, adverse drug reaction
clarithromycin: DT, drug therapy
dirithromycin: DT, drug therapy
levofloxacin: DT, drug therapy
lomefloxacin: DT, drug therapy
nalidixic acid: DT, drug therapy
norfloxacin: DT, drug therapy
ofloxacin: DT, drug therapy
sparfloxacin: DT, drug therapy
trovafloxacin: DT, drug therapy
amikacin: DT, drug therapy
gentamicin: DT, drug therapy
kanamycin: DT, drug therapy
neomycin: DT, drug therapy
netilmicin: DT, drug therapy
spectinomycin: DT, drug therapy
streptomycin: DT, drug therapy
tobramycin: DT, drug therapy
vancomycin: AE, adverse drug reaction
vancomycin: DT, drug therapy
ciprofloxacin
tobramycin sulfate
alatrofloxacin
enoxacin
meticillin
carindacillin
amoxicillin plus clavulanic acid
sultamicillin
orpeneed
beepen
penicillin v
bacampicillin
cloxacillin
dicloxacillin
cefapirin
cefamandole nafate
cefmetazole
piperacillin plus tazobactam
timentin

CAS REGISTRY NO.: (benzathine penicillin) 1538-09-6; (procaine penicillin) 54-35-3, 6130-64-9; (penicillin g sodium) 69-57-8; (penicillin v potassium) 132-98-9; (penicillin g potassium) 113-98-4, 1406-08-2; (penicillin g) 1406-05-9, 61-33-6; (amoxicillin) 26787-78-0, 61336-70-7; (ampicillin) 69-52-3, 69-53-4, 7177-48-2, 74083-13-9, 94586-58-0; (nafcillin) 147-52-4, 985-16-0; (oxacillin) 1173-88-2, 66-79-5, 7240-38-2; (carbenicillin) 17230-86-3, 4697-36-3, 4800-94-6; (mezlocillin) 42057-22-7, 51481-65-3; (piperacillin) 59703-84-3, 61477-96-1; (ticarcillin) 29457-07-6, 34787-01-4, 4697-14-7; (clavulanic acid) 58001-44-8; (sulbactam) 68373-14-8; (tazobactam) 93528-38-2; (cefadroxil) 50370-12-2; (cefazolin) 25953-19-9, 27164-46-1; (cefalexin) 15686-71-2, 23325-78-2; (cefalotin) 153-61-7, 58-71-9; (cefradine) 38821-53-3, 57584-26-6; (cefaclor) 53994-73-3; (cefamandole) 30034-03-8, 34444-01-4; (cefonicid) 61270-58-4, 61270-78-8; (cefotetan) 69712-56-7, 74356-00-6; (cefoxitin) 33564-30-6, 35607-66-0; (cefprozil) 92665-29-7; (cefuroxime) 55268-75-2, 56238-63-2; (cefuroxime axetil) 64544-07-6; (cefepime) 88040-23-7; (cefixime) 79350-37-1; (cefoperazone) 62893-19-0, 62893-20-3; (cefotaxime) 63527-52-6, 64485-93-4; (cefpodoxime proxetil) 87239-81-4; (ceftazidime) 72558-82-8; (ceftibuten) 97519-39-6;

(ceftizoxime) 68401-81-0, 68401-82-1; (ceftriaxone) 73384-59-5, 74578-69-1; (loracarbef) 76470-66-1; (cilastatin plus imipenem) 92309-29-0; (meropenem) 96036-03-2; (aztreonam) 78110-38-0; (erythromycin) 114-07-8, 70536-18-4; (azithromycin) 83905-01-5; (clarithromycin) 81103-11-9; (dirithromycin) 62013-04-1; (levofloxacin) 100986-85-4, 138199-71-0; (lomefloxacin) 98079-51-7; (nalidixic acid) 389-08-2; (norfloxacin) 70458-96-7; (ofloxacin) 82419-36-1; (sparfloxacin) 111542-93-9; (trovafloxacin) 146836-84-2; (amikacin) 37517-28-5, 39831-55-5; (gentamicin) 1392-48-9, 1403-66-3, 1405-41-0; (kanamycin) 11025-66-4, 61230-38-4, 8063-07-8; (neomycin) 11004-65-2, 1404-04-2, 1405-10-3, 8026-22-0; (netilmicin) 56391-56-1, 56391-57-2; (spectinomycin) 1695-77-8, 21736-83-4, 23312-56-3; (streptomycin) 57-92-1; (tobramycin) 32986-56-4; (vancomycin) 1404-90-6, 1404-93-9; (ciprofloxacin) 85721-33-1; (tobramycin sulfate) 49842-07-1; (alatrofloxacin) 157605-25-9; (enoxacin) 74011-58-8; (meticillin) 132-92-3, 38882-79-0, 61-32-5; (carindacillin) 26605-69-6, 35531-88-5; (amoxicillin plus clavulanic acid) 74469-00-4; (sultamicillin) 76497-13-7; (penicillin v) 87-08-1; (bacampicillin) 37661-08-8, 50972-17-3; (cloxacillin) 61-72-3, 642-78-4; (dicloxacillin) 13412-64-1, 3116-76-5, 343-55-5; (cefapirin) 21593-23-7, 24356-60-3; (cefamandole nafate) 42540-40-9; (cefmetazole) 56796-20-4, 56796-39-5; (timentin) 86482-18-0

CHEMICAL NAME: Trovan; Cipro; Pentrex; Levaquin; Maxaquin; Negram; Noroxin; Floxin; Zagam; Amikin; Garamycin; Kantrex; Mycifradin; Nebcin; Netromycin; Trobicin; Alatrofloxacin; Ciprofloxacin; Enoxacin; Staphcillin; Unipen; Nafcil; Prostaphlin; Geocillin; Mezlin; Pipracil; Ticar; Augmentin; Unasyn; Bicillin l a; Orpeneed; Pfizerpen; Beepen; **Pen vee**; Amoxil; Omnipen; Spectrobid; Cloxapen; Dycill; Duricef; Ancef; Keflex; Keflin; Cefadyl; Velosef; Ceclor; Mandol; Zefazone; Monocid; Cefotan; Mefoxin; Ceftin; Maxipime; Suprax; Cefobid; Claforan; Vantin; Fortaz; Cedax; Cefizox; Rocephin; Lorabid; Primaxin; Merrem; Azactam; Zithromax; Biaxin; Dynabac; Zosyn; Timentin; Nallpen; Pathocil; Tegopen; Wymox; Trimox; Ledercillin vk; Pentids; Wycillin

L16 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1992:531480 CAPLUS

DOCUMENT NUMBER: 117:131480

TITLE: Synthesis and antiviral evaluation of N-carboxamidine-substituted analogs of 1-.beta.-D-ribofuranosyl-1,2,4-triazole-3-carboxamidine hydrochloride.

AUTHOR(S): Gabrielsen, Bjarne; Phelan, Michael J.; Barthel-Rosa, Luis; See, Cathy; Huggins, John W.; Kefauver, Deborah F.; Monath, Thomas P.; Ussery, Michael A.; Chmurny, Gwendolyn N.; et al.

CORPORATE SOURCE: U.S. Army Med. Res. Inst. Infect. Dis., Frederick, MD, 21702, USA

SOURCE: Journal of Medicinal Chemistry (1992), 35(17), 3231-8
CODEN: JMCMAR; ISSN: 0022-2623

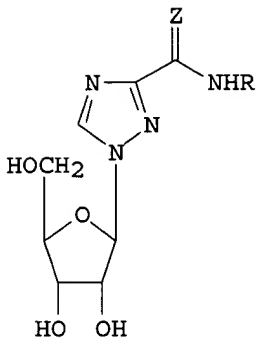
DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 33-9 (Carbohydrates)
Section cross-reference(s): 1, 34

OTHER SOURCE(S): CASREACT 117:131480

GRAPHIC IMAGE:



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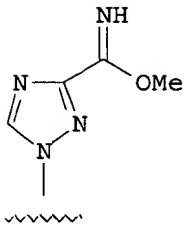

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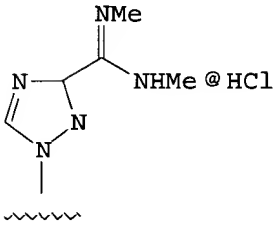

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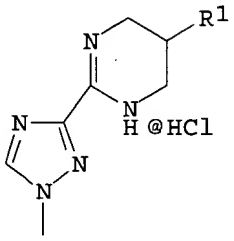

IV

ABSTRACT:
Ten, hitherto unreported, analogs of 1-(.beta.-D-ribofuranosyl)-1,2,4-triazole-3-carboxamidine hydrochloride (I.cntdot.HCl; R = H, Z = NH; ribamidine) and Me carboximidate II were synthesized. These include the N-cyano (I; R = CN, Z = NH), N-alkyl (I; R = Me, Bu, octyl, Z = NH), N-amino acid [I; R = CH2CO2H, CH(CO2H)CH2CONH2, CH(CO2H)CH2CH2CONH2, Z = NH], N,N'-disubstituted III and IV (R1 = H, OH), and the N-methylated carboxamide analogs I (R = Me, Z = O) of ribavirin. In addn., a new facile synthesis of carboxamidine I.cntdot.HCl (R = H, Z = NH) was also developed. All compds. were evaluated for biol. activity against the following RNA viruses: Punta Toro (PT) and sandfly fever (SF) viruses (bunyaviruses); Japanese encephalitis (JE), yellow fever (YF), and dengue-4 viruses (flaviviruses); parainfluenza type 3 (PIV3), respiratory syncytial virus (RSV), and measles viruses (paramyxoviruses); influenza A and influenza B viruses (orthomyxoviruses); Venezuelan equine encephalomyelitis virus (**VEE**, alphavirus); human immunodeficiency virus type-1 (HIV-1, lentivirus); the DNA-contg. vaccinia (VV) virus (poxvirus); and adeno type 5 (Ad5) viruses. All of the compds. except for I (R = CN, Z = NH) and IV exhibited activity against the bunyaviruses such as that obsd. with I.cntdot.HCl (R = H, Z = NH); however, higher IC50 values were generally obsd. Glycine analog I (R = CH2CO2H, Z = NH) showed activity in PT-virus-infected mice in terms of increased survivors and decreased markers of viral pathogenicity. Carboxamidine I.cntdot.HCl (R = H, Z = NH), carboximidate II, and di-Me amidine III exhibited activity against dengue type-4 virus. Monomethyl amidine I.cntdot.HCl (R = Me, Z = NH) demonstrated activity against RSV, PIV/3, and, to a lesser extent, influenza A and B. Activity of I.cntdot.HCl (R = Me, Z = NH) generally required higher IC50 values than unsubstituted I.cntdot.HCl (R = H, Z = NH). The latter exhibited hitherto unreported activity against RSV; therapeutic indexes for I.cntdot.HCl (R = H, Z = NH) against RSV and PIV3 were >64 and >21. No substantial in vitro activity was obsd. for any of the compds. tested against Ad5, measles, JE, YF, ***VEE*** , or HIV-1. In addn., evidence is presented which argues in favor of a distinct antiviral mechanism of action for carboxamidines, e.g. III, in contrast to a role as a carboxamide precursor.

SUPPL. TERM: ribavirin analog synthesis antiviral pathogenicity; triazolecarboxamidine ribofuranoside synthesis antiviral; AIDS **inhibitor** triazolecarboxamidine ribofuranoside; HIV **inhibitor**

triazolecarboxamidine ribofuranoside; virucide
triazolecarboxamidine ribofuranoside synthesis;
carboxamidine analog ribavirin synthesis antiviral;
ribamidine synthesis virucide

INDEX TERM: Acquired immune deficiency syndrome
(inhibitors, ribavirin carboximidate analogs, inactive)

INDEX TERM: Virucides and Virustats
(ribavirin carboximidate analogs)

INDEX TERM: Nucleotides, preparation
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(analogs, ribavirin carboximidate, prepn. and antiviral activity of)

INDEX TERM: Toxicity
(cytotoxicity, of ribavirin carboximidate analogs)

INDEX TERM: Virus, animal
(human immunodeficiency 1, inhibitors, ribavirin carboximidate analogs, inactive)

INDEX TERM: 40371-99-1
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis and imidation of, with ammonium chloride)

INDEX TERM: 36791-04-5DP, Ribavirin, analogs 142633-76-9P
142633-77-0P 142633-78-1P 142633-79-2P 142633-80-5P
142633-81-6P 142633-82-7P 142633-83-8P 142633-84-9P
142633-85-0P 142633-86-1P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antiviral activity of)

INDEX TERM: 40372-00-7P
ROLE: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn., reactions, and antiviral activity of)

INDEX TERM: 120362-25-6
ROLE: RCT (Reactant); RACT (Reactant or reagent)
(reactions of, in prepn. of ribavirin carboximidate analogs)

L16 ANSWER 9 OF 10 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:344789 BIOSIS
DOCUMENT NUMBER: BA94:37014
TITLE: SELECTIVE INHIBITION OF ARTHROPOD-BORNE AND ARENAVIRUSES IN-VITRO BY 3' FLUORO-3'-DEOXYADENOSINE.
AUTHOR(S): SMEE D F; MORRIS J L B; BARNARD D L; VAN AERSCHOT A
CORPORATE SOURCE: DEP. ANIM. DAIRY VET. SCI., UTAH STATE UNIV., LOGAN, UT 84322-5600.
SOURCE: ANTIVIRAL RES, (1992) 18 (2), 151-162.
CODEN: ARSRDR. ISSN: 0166-3542.
FILE SEGMENT: BA; OLD
LANGUAGE: English
ABSTRACT:
A novel nucleoside analog, 3'-fluoro-3'-deoxyadenosine (3'F3'dAdo), was evaluated for antiviral activity against several arthropod-borne and arenaviruses in Vero cell culture. The following 50% inhibitory concentrations (EC50) of virus plaque formation were obtained against the test viruses: Semliki Forest (10.3 .mu.M) and Venezuelan equine encephalitis (5.3 .mu.M) alphaviruses, lymphocytic choriomeningitis (7.7 .mu.M) and Pichinde (> 32 .mu.M) arenaviruses, Punta Toro (> 32 .mu.M) and San Angelo (1.6 .mu.M) bunyaviruses, banzi flavivirus (4.0 .mu.M), and Colorado tick fever orbivirus (0.6 .mu.M). By comparison, the broad-spectrum antiviral agent ribavirin was active against lymphocytic choriomeningitis (18 .mu.M), Pichinde (24 .mu.M),

Punta Toro (114 .mu.M), and SanAngelo (99 .mu.M) viruses, but was less active against the other 4 viruses (> 200 .mu.M). Vero cell proliferation and thymidine and uridine incorporation into replicating Vero cells were inhibited by 50% with 3'F3'dAdo concentrations of 36, 45, and 32 .mu.M, respectively. In virus yield reduction assays, increasing the multiplicity of infections of Semliki Forest and Venezuelan equine encephalitis viruses reduced the inhibitory activity of 3'F3'dAdo. Using the same assay, 3'F3'dAdo was found to enhance Punta Toro virus replication up to 5-fold relative to the untreated control. By adding the nucleoside transport **inhibitor** nitrobenzylthioinosine (100 .mu.M) to the culture medium, antiviral activity against the two alphaviruses was eliminated, indicating that 3'F3'dAdo uses the nucleoside transport system for cell entry. When actinomycin D (5 .mu.M) was used to greatly suppress cellular RNA synthesis in Semliki Forest virus-infected and uninfected cells, 3'F3'dAdo preferentially inhibited viral RNA synthesis. The results of these studies indicate 3'F3'dAdo is a selective ***inhibitor*** of most of the viruses tested and should be a promising candidate for in vivo evaluations.

CONCEPT CODE: Cytology and Cytochemistry - Animal *02506
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines 10062
Pathology, General and Miscellaneous - Therapy 12512
Metabolism - Nucleic Acids, Purines and Pyrimidines *13014
Pharmacology - General *22002
Pharmacology - Drug Metabolism; Metabolic Stimulators *22003
Toxicology - Pharmacological Toxicology 22504
Virology - Animal Host Viruses *33506
Medical and Clinical Microbiology - Virology 36006
Chemotherapy - Antiviral Agents *38506

BIOSYSTEMATIC CODE: Arenaviridae 02212
Bunyaviridae 02216
Reoviridae - animal host only 02236
Togaviridae 02252
Cercopithecidae 86205

INDEX TERMS: Miscellaneous Descriptors
ARBOVIRUS PUNTA TORO VIRUS SEMLIKI FOREST VIRUS PICHINDE VIRUS **VENEZUELAN EQUINE ENCEPHALITIS VIRUS** LYMPHOCYTIC CHORIOMENINGITIS VIRUS SAN ANGELO VIRUS BANZI VIRUS COLORADO TICK FEVER VIRUS VERO CELLS RIBAVIRIN ANTIVIRAL-DRUG PHARMACOKINETICS PHARMACODYNAMICS CELL UPTAKE MECHANISM NUCLEOSIDE TRANSPORT SYSTEM VIRAL RNA SYNTHESIS **INHIBITOR** CYTOTOXICITY MULTIPLICITY OF INFECTION DEPENDENT

REGISTRY NUMBER: 36791-04-5 (RIBAVIRIN)

L16 ANSWER 10 OF 10 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 91320774 EMBASE
DOCUMENT NUMBER: 1991320774
TITLE: The penicillins.
AUTHOR: Wright A.J.; Wilkowske C.J.
CORPORATE SOURCE: Mayo Clinic Proceedings, Siebens Building, Rochester, MN 55905, United States
SOURCE: Mayo Clinic Proceedings, (1991) 66/10 (1047-1063).
ISSN: 0025-6196 CODEN: MACPAJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT:
The penicillin family of antibiotics remains an important part of our

antimicrobial armamentarium. In general, these agents have bactericidal activity, excellent distribution throughout the body, low toxicity, and efficacy against infections caused by susceptible bacteria. The initial introduction of aqueous penicillin G for treatment of streptococcal and staphylococcal infections was an important pharmacologic landmark. The emergence of penicillinase-producing Staphylococcus aureus prompted the development of the penicillinase-resistant penicillins (for example, methicillin, oxacillin, and nafcillin), in which an acyl side chain prevented disruption of the .beta.-lactamase ring. Subsequently, the aminopenicillins (such as ampicillin and amoxicillin) were developed because of the need for gram-negative antimicrobial activity. Their spectrum included Escherichia coli, Proteus mirabilis, Shigella, Salmonella, Listeria, Haemophilus, and Neisseria. The search for a penicillin with additional antimicrobial activity against the Enterobacteriaceae and Pseudomonas aeruginosa led to the development of the carboxypenicillins (carbenicillin, ticarcillin, and temocillin) and the ureidopenicillins (mezlocillin, azlocillin, piperacillin, and apalcillin). Finally, the combination of a .beta.-lactamase **inhibitor** (clavulanic acid or sulbactam) and an aminopenicillin or ticarcillin has further extended their antibacterial spectra. The development of an ideal penicillin that is rapidly bactericidal, nonsensitizing, nontoxic, bioavailable, resistant to .beta.-lactamase, and without inoculum effect and that has a high affinity for penicillin-binding proteins remains the goal.

CONTROLLED TERM:

Medical Descriptors:
*antimicrobial therapy
conference paper
priority journal
Drug Descriptors:
*penicillin derivative
amoxicillin
amoxicillin plus clavulanic acid
ampicillin
apalcillin
azlocillin
bacampicillin
bactocill
benzathine penicillin
carbenicillin
clavulanic acid
cloxacillin
cyclacillin
dicloxacillin
foramdinocillin
hetacillin
mecillinam
meticillin
mezlocillin
nafcillin
oxacillin
pathocill
penapar
penicillin g
penicillin g potassium
penicillin v
pheneticillin
piperacillin
pivmecillinam
procaine penicillin
sulbactam
sultamicillin
temocillin
ticarcillin
timentin
unclassified drug

CAS REGISTRY NO.: (amoxicillin) 26787-78-0, 61336-70-7; (amoxicillin plus clavulanic acid) 74469-00-4; (ampicillin) 69-52-3, 69-53-4, 7177-48-2, 74083-13-9, 94586-58-0; (apalcillin) 58795-03-2, 63469-19-2; (azlocillin) 37091-65-9, 37091-66-0; (bacampicillin) 37661-08-8, 50972-17-3; (benzathine penicillin) 1538-09-6; (carbenicillin) 17230-86-3, 4697-36-3, 4800-94-6; (clavulanic acid) 58001-44-8; (cloxacillin) 61-72-3, 642-78-4; (cyclacillin) 3485-14-1; (dicloxacillin) 13412-64-1, 3116-76-5, 343-55-5; (hetacillin) 3511-16-8, 5321-32-4; (mecillinam) 32887-01-7; (meticillin) 132-92-3, 38882-79-0, 61-32-5; (mezlocillin) 42057-22-7, 51481-65-3; (nafcillin) 147-52-4, 985-16-0; (oxacillin) 1173-88-2, 66-79-5, 7240-38-2; (penicillin g) 1406-05-9, 61-33-6; (penicillin g potassium) 113-98-4, 1406-08-2; (penicillin v) 87-08-1; (pheneticillin) 132-93-4, 147-55-7; (piperacillin) 59703-84-3, 61477-96-1; (pivmecillinam) 32886-97-8, 32887-03-9; (procaine penicillin) 54-35-3, 6130-64-9; (sulbactam) 68373-14-8; (sultamicillin) 76497-13-7; (temocillin) 61545-06-0, 66148-78-5; (ticarcillin) 29457-07-6, 34787-01-4, 4697-14-7; (timentin) 86482-18-0

CHEMICAL NAME: Pentids; Pfizerpen; Wycillin; Duracillin; Bicillin; Permapen; **Pen vee**; V cillin; Broxil; Syncillin; Maxipen; Staphcillin; Prostaphlin; Unipen; Nafcil; Nallpen; Tegopen; Cloxapen; Dynapen; Dycill; Polycillin; Omnipen; Amoxil; Polymox; Spectrobid; Versapen; Cyclapen; Geopen; Ticar; Mezlin; Pipracil; Coactin; Augmentin; Timentin; Unasyn; Penapar; Bactocill; Pathocill; Wymox